Zacks Small-Cap Research

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# Motif Bio Plc

**MTFB - NASDAQ**

***MTFB: Positive Results From Second Phase 3 Study of Iclaprim; NDA Filing Anticipated in 1Q18…***

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 (10/05/2017) | $11.75 |
| **Valuation** | **$31.00** |

## INITIATION

On October 4, 2017, Motif Bio Plc announced positive results from REVIVE-2, the second Phase 3 trial testing the company's lead asset, iclaprim, in patients with acute bacterial skin and skin structure infections (ABSSSI). The results mirrored those reported from REVIVE-1, which were previously announced in April 2017, and showed iclaprim achieved the primary endpoint of non-inferiority compared to vancomycin at both the early time point and the test of cure endpoint. Iclaprim was well tolerated, with a very similar adverse event profile to vancomycin. With two positive Phase 3 clinical trials completed, we anticipate Motif filing for approval in the first quarter of 2018, and with a six-month regulatory review iclaprim could be approved by the FDA before the end of 2018.

## SUMMARY DATA

| | |
|---|---|
| **52-Week High** | **$11.75** |
| **52-Week Low** | **$5.29** |
| **One-Year Return (%)** | **N/A** |
| **Beta** | **N/A** |
| **Average Daily Volume (sh)** | **11,461** |
| **Shares Outstanding (mil)** | **13** |
| **Market Capitalization ($mil)** | **$130** |
| **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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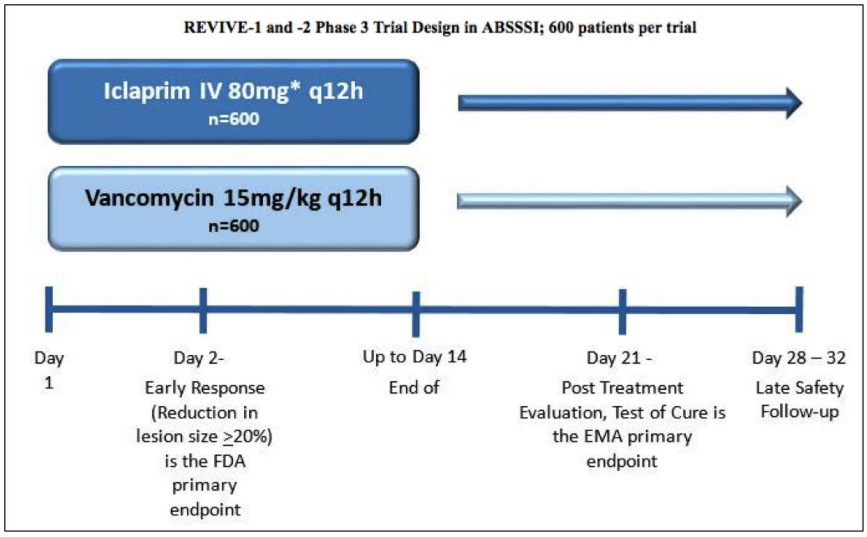
## WHAT'S NEW

**Business Update**

On October 4, 2017, Motif Bio (MTFB) announced positive topline results from REVIVE-2, the second Phase 3 clinical trial of iclaprim in patients with acute bacterial skin and skin structure infections (ABSSSI). These results follow on the previously announced positive topline results from REVIVE-1. With positive results from two Phase 3 clinical trials, we anticipate Motif filing a New Drug Application (NDA) in the first quarter of 2018 and with a six-month review (based on Fast Track status), iclaprim could be approved for the treatment of ABSSSI before the end of 2018.

*REVIVE-2 Results*

The REVIVE Phase 3 program for iclaprim in the treatment of ABSSSI included two randomized, double blind clinical trials (REVIVE-1 and REVIVE-2). Each 600-patient trial had two arms, with patients receiving either 80 mg iclaprim or 15 mg/kg vancomycin every 12 hours. The trials evaluated both the FDA endpoint of an early clinical response of at least 20% reduction in a lesion size at 48-72 hours and the EMA endpoint of clinical cure at test of cure one to two weeks after antibiotic treatment ends. The following diagram summarizes the REVIVE Phase 3 clinical trials.




*Source*: Motif Bio Plc

In REVIVE-2, iclaprim achieved the primary endpoint of non-inferiority (10% margin) compared to vancomycin at the early time point (ETP; 48-72 hours after the start of administration of the study drug) and at the test of cure (TOC) endpoint (7 to 14 days after study drug discontinuation), as shown in the following table. There was a slight decrease in efficacy for both compounds when comparing the results of REVIVE-1 and REVIVE-2, however on the conference call to discuss the results management indicated that this is likely within the normal variation seen in clinical trials and the topline results did not offer any evidence for other explanations.

| Timepoint | Endpoint | Iclaprim N=295 | Vancomycin N=305 | % Difference (95% CI) |
|---|---|---|---|---|
| ETP (primary endpoint) | Early Clinical Response (ECR) | 231 (78.3%) | 234 (76.7%) | 1.58 (-5.10, 8.26) |
| TOC | Clinical cure | 230 (78.0%) | 237 (77.7%) | 0.26 (-6.39, 6.91) |

*Source*: Motif Bio Plc

Motif also announced the results from pre-specified secondary endpoints. Demonstration of resolution or near resolution at end of therapy was seen in 54.6% of iclaprim-treated patients compared to 55.4% of vancomycin-treated patients (95% CI: -8.80% to 7.13%). Using a modified clinical cure endpoint defined by >90% reduction in lesion size, no increase in lesion size since ETP, and no requirement for additional antibiotics, clinical cure was seen in 71.9% of iclaprim-treated patients compared to 70.5% of vancomycin-treated patients (95% CI: -5.88% to 8.62%). The company is planning to present a full analysis of the data at a future scientific conference.

Just as in REVIVE-1, iclaprim was well tolerated in REVIVE-2, with an adverse event profile very similar to vancomycin and most (75%) adverse events classified as mild.

| | Iclaprim N=299 | Vancomycin N=302 |
|---|---|---|
| TEAEs (Treatment Emergent Adverse Events)* | 140 (46.8%) | 133 (44.0%) |
| Study drug related TEAEs | 42 (14.0%) | 39 (12.9%) |
| TEAEs leading to discontinuation of study drug | 16 (5.4%) | 17 (5.6%) |
| TEAE related SAEs (Serious AEs) | 14 (4.7%) | 12 (4.0%) |
| Deaths | 0 | 1 |

*Source*: Motif Bio Plc

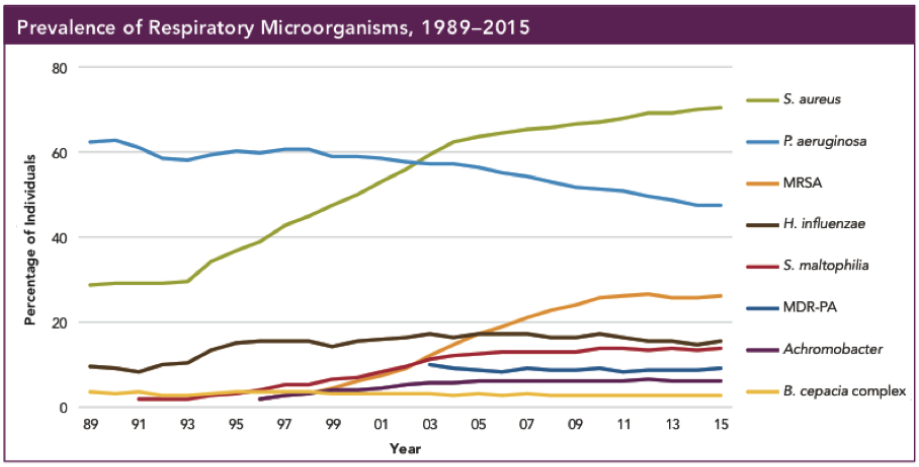
*FDA Grants Iclaprim ODD*

On September 15, 2017, Motif announced that the U.S. FDA has granted iclaprim Orphan Drug Designation (ODD) for the treatment of lung infections in patients with cystic fibrosis (CF) caused by *Staphylococcus aureus*. A number of incentives accompany orphan designation, including various development incentives, tax credits for clinical testing, waiver of user fees, and potentially up to seven years of market exclusivity for the given indication.

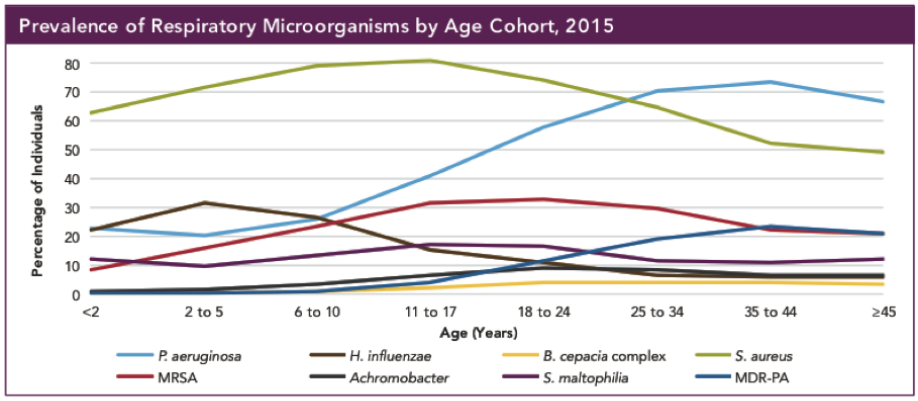
CF is an autosomal recessive genetic disorder that affects close to 30,000 individuals in the U.S. and a total of 70,000 people worldwide. The hallmark of CF is a thick, sticky mucus build up in various organs throughout the body. Typically, mucus is a slippery, water substance produced by tissues that line organs and body cavities, such as the lungs and nose. However, due to abnormal sodium and chloride transport in the lungs, pancreas, liver, and digestive tract, patients suffering from CF have mucus that is thick and sticky and leads to blockages of the airways in the lungs and ducts in the pancreas (Boucher, 2004). The name refers to the characteristic scarring (fibrosis) and cyst formation seen in the pancreas.

The most serious complication associated with the disease is difficulty in breathing due to recurrent lung infections. Lung disease in patients with CF results from airway blockage and resulting inflammation. The build up of mucus is an ideal environment for bacteria to grow, and the inflammation and repeated infections result in injury and structural changes to the lungs. Early stages of the disease are characterized by excessive coughing, phlegm production and shortness of breath. These symptoms are exacerbated when the overgrowth of bacteria leads to pneumonia. *Staphylococcus aureus* and *Pseudomonas aeruginosa* are the two most common organisms that cause lung infections in CF patients. Lung infections are responsible for the deaths of 80% of CF patients (O'Sullivan *et al*., 2009).

The following two graphs are taken from the Cystic Fibrosis Foundation 2015 Patient Registry Report, which reports the prevalence of different bacterial pathogens for CF patients. As the first graph shows, the prevalence of *S. aureus* has been increasing for a number of years, with a significant proportion of the *S. aureus* infections being caused by methicillin resistant *S. aureus* (MRSA). *S. aureus* is the causative pathogen in the majority of CF patients up until about the age of 25.




*Source*: CFF Patient Registry 2015




*Source*: CFF Patient Registry 2015

On July 6, 2017, Motif announced three posters will be presented at the Infectious Diseases Week Annual Meeting, which is taking place in San Diego, CA from Oct. 4-8, 2017. One of the posters will present results from an *in vivo* study of iclaprim and vancomycin using a strain of MRSA in an animal model of chronic infection that mimics the pathophysiology observed in CF patients, an area that the company will be pursuing in the near future.

*Additional Upside Possible from HABP/VABP*

In addition to ABSSI and CF, Motif is also planning to conduct a study of iclaprim in patients with hospital acquired bacterial pneumonia (HABP) and ventilator associated bacterial pneumonia (VBAP). Motif has produced data showing that iclaprim's concentration in epithelial lining fluid (ELF) and alveolar macrophages (AM) is elevated in comparison to serum levels. The concentration of iclaprim in ELF and AM was 20 to 30 times the serum concentration, which could lead to positive outcomes for treating lung infections. Motif has put together a Phase 3 clinical trial plan (INSPIRE) for iclaprim in HABP/VABP. It will be a randomized, double blind comparator controlled international study comparing the safety and efficacy of iclaprim to linezolid in the treatment of HABP, including VABP. Treatment with both iclaparim and linezolid is expected to be 7 to 14 days. A total of approximately 720 subjects will be studied with a non-inferiority margin of -10%. The primary endpoint of the study will be all cause mortality at Day 28, with a key secondary endpoint of clinical cure at one to two weeks after ending antibiotic treatment.

**Financial Update**

On September 29, 2017, Motif announced financial results for the first half of 2017. Net loss for the first six months of 2017 was $29.7 million, and consisted of $23.8 million in R&D expenses and $4.4 million in G&A expenses. This compared to $12 million in R&D expenses and $1.9 million in G&A expenses in the first six months of 2016. The increase in R&D expenses was primarily due to an increase in contract research organization expenses and personnel related expenses. The increase in G&A expenses was primarily due to increased personnel expenses and costs associated with being publicly traded on the NASDAQ Capital Market, which began in Nov. 2016.

Motif exited the first half of 2016 with approximately $29.5 million in cash and cash equivalents and as of September 22, 2017, Motif had cash and cash equivalents of approximately $18.1 million. This is primarily attributable to a private placement in the United Kingdom the company conducted in June 2017 that resulted in net proceeds of $23.7 million from the sale of 66.67 million ordinary shares at 30 pence per share. As of June 30, 2017, Motif had approximately 262.9 million 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's ordinary shares. When factoring in the approximately 27.9 million stock options and 47.5 million warrants, the company has a fully diluted share count of approximately 338.3 million (equivalent to 16.9 million ADSs).

## Conclusion

The positive results from REVIVE-2 will allow Motif to proceed with a New Drug Application (NDA), which we anticipate being filed 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 due to iclaprim having Fast Track designation. 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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## HISTORICAL STOCK PRICE




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