at a glance™

Motif Bio has completed two successful pivotal Phase 3 clinical trials of iclaprim, a well differentiated antibiotic candidate targeting MRSA. The first of two Phase 3 trials reported positive results in April of this year. The second Phase 3 reported positive results in October. Both trials tested iclaprim vs. vancomycin in acute bacterial skin and skin structure infections, one of the most common serious infections. A New Drug Application (NDA) is scheduled to be filed with the FDA 1Q18, with commercial launch into a multi-billion-dollar market opportunity planned for 1H19.

Key Considerations

- **Motif Bio is a late-stage bio pharma company that's developing iclaprim (*ick-la-prim*), a novel antibiotic candidate, for three indications at present, all addressing major unmet needs in a billion-dollar-plus market.**
- **The most advanced indication is in ABSSSI – acute bacterial skin and skin structure infections.**
- **The antibiotics currently used to treat these infections can be problematic in the roughly 26 percent of the 3.6 million ABSSSI patients hospitalized each year in the U.S. who also have damaged kidneys and often diabetes as well.**
- **Iclaprim's safety and efficacy profile appears ideally suited for this population since it has not been associated with kidney damage or low blood sugar.**
- **Both ABSSSI Phase 3 trials were successful. The study designs were identical.**
- **The company expects to file for FDA approval in ABSSSI 1Q18, paving the way for a U.S. commercial launch in 1H19. The addressable market for renal impaired ABSSSI patients alone is put at $2.8 billion.**
- **A separate Phase 3 program has been established for iclaprim in hospital-acquired bacterial pneumonia, including ventilator-associated bacterial pneumonia. The addressable market is estimated at $1.7 billion.**
- **Studies have shown iclaprim concentrates in the lungs following intravenous administration, a feature that may add to iclaprim's effectiveness in treating bacterial lung infections. Efficacy has been demonstrated in a Phase 2 trial in patients with HABP.**
- **The third potential indication for iclaprim is in MRSA pneumonia in patients with cystic fibrosis. The FDA granted Orphan Drug Designation to iclaprim for this indication in September 2017.**
- **Iclaprim was granted QIDP (Qualified Infectious Disease Product) designation by the U.S. FDA, which includes Fast Track Status and Priority Review upon acceptance of the NDA (New Drug Application). QIDP also provides 10 years of market exclusivity from the date of approval.**
- **Motif Bio completed a $20 million debt facility with Hercules Capital in November 2017 and has drawn down $15 million. The remaining $5 million will be available upon achievement of certain milestones anticipated in 2018, or at the lender's discretion.**

Motif BioSciences Inc.
(Nasdaq ADS: MTFB)

Recent ADS Price:	$9.30
Recent AIM Exch.:	35.00 pence
(1 ADS equals 20 AIM shares)	
Approx. Mkt Cap:	$126 Million
Fiscal Year Ends:	December 31

Key institutional holders (%)
Invesco (25.2), Amphion Group (14.1), Sand Grove (6.1), Aviva (3.5)

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Overview

Antibiotics are designed to kill bacteria. They don't typically rely on complex or sequential biological interactions to do their job, as is often the case with receptor-driven anti-cancer compounds, arthritis treatments, or dementia drugs, to name a few.

If an antibiotic kills bacteria in a petri dish, it will likely kill them in an animal and if it kills them in an animal it will kill them in a human. After that's established, the questions center on how fast, how complete, and how safe.

Beyond that, an antibiotic's mechanism of action can play a key role in its long-term performance.

The fact of the matter is that many of today's antibiotics have been used so frequently and for so long in so many people that the bugs have learned to out-smart the drugs. This has created the era of the

Notable & Upcoming

-3Q17 - Motif Bio Investor & Analyst Day, NYC

-3Q17 - US FDA granted Orphan Drug Designation to iclaprim for *Staphylococcus aureus* lung infections in cystic fibrosis patients

-4Q17 - Top-line results reported from second of two successful Motif Bio iclaprim Phase 3 clinical trials in ABSSSI

-4Q17 - New animal data relevant to pulmonary infections that mimics cystic fibrosis-like conditions reported at ID Week, showing improvements over vancomycin in survival and reduction of bacterial colony forming units

-1Q18 - NDA submission to FDA scheduled for ABSSSI indication

-4Q18 - FDA decision to market expected

so-called 'Super Bugs', bacteria that have become resistant to drugs that once killed them. In the land of the Super Bugs, MRSA (Methicillin-resistant *Staphylococcus aureus*) is one of the most common bacteria causing serious and life-threatening infections.

Fortunately, iclaprim's mechanism of action is employed in only one other antibiotic, trimethoprim, which is mainly prescribed in combination with a sulfonamide for bladder, chest and upper respiratory tract infections.

Iclaprim is the first antibiotic candidate with the mechanism similar to trimethoprim that is potent enough to be prescribed on its own without the need for a sulfonamide. The sulfonamide component of the combination is fraught with side effects, which limits its use.

Iclaprim has been administered to more than 1300 patients and healthy volunteers.

Most importantly, iclaprim has been well tolerated in patients with diabetes or renal impairment. Standard-of-care vancomycin, the comparator antibiotic in iclaprim's Phase 3 program, is known to potentially worsen kidney damage. Its use in patients with existing kidney damage requires costly and time-consuming monitoring, adjustments in dosing, and often leads to extended hospital stays.

About Iclaprim

Iclaprim is a diaminopyrimidine antibiotic that belongs to a class of compounds called dihydrofolate reductase inhibitors, or DHFRis. One drug in this class has been approved as an antibiotic - trimethoprim.

That's good news for two reasons. The drug's approval validates the DHFRi mechanism of action and its safety. Secondly, bacteria that have developed resistance to other mechanisms which include many antibiotics such as penicillins, cephalosporins, tetracyclines, macrolides etc., may be killed by iclaprim because it works in a different way.

In vitro studies have demonstrated that iclaprim exhibits greater potency against *Staphylococcus aureus*, including MRSA and kills bacteria twice as fast as vancomycin, the comparator in the current Phase 3 trials.

Motif Bio acquired rights to iclaprim in 2015, optimized the dosing regimen, and in March 2016 initiated two Phase 3 clinical trials to study the safety and efficacy of iclaprim under the new FDA criteria for ABSSSI.

A 30 percent improvement in iclaprim's ability to kill bacteria was achieved by optimizing the dosing regimen from a weight-based dose to a fixed dose with a longer infusion.

In prescribing terms, this meant changing from an iclaprim dose of 0.8 milligram per kilogram (1 kilogram is 2.2 lbs) of body weight twice daily to a fixed 80 milligram dose for each patient twice daily, regardless of body weight, infused from 30 minutes to 120 minutes.

Iclaprim in ABSSSIs

In October 2017 Motif Bio announced that the second of two Phase 3 clinical trials of iclaprim in ABSSSIs achieved its primary endpoint of non-inferiority (10% margin) compared to vancomycin, the current standard of care antibiotic, at the early time point, 48-72 hours after the start of administration of the study drug.

The first Phase 3 reported similar top-line results in April 2017.

Iclaprim was well-tolerated in both trials. Fuller details on the results are available at www.motifbio.com.

Both Phase 3s were global, multi-center, double-blinded trials, each enrolling 600 patients randomized 50-50 to iclaprim or vancomycin. Their protocols are identical.

The expected approval of iclaprim will be for treating patients with ABSSSIs (major abscesses, cellulitis, surgical site infections), caused principally by MRSA. Motif Bio intends to focus on those patients who require hospitalization, are at high risk of complications, difficult to treat with today's standard of care antibiotics and who suffer from kidney damage, with or without diabetes.

As such, it would potentially take prescriptions away from standard of care antibiotics such as vancomycin and linezolid, providing access to an attractively-sized market that's expected to expand over time.

As a potential first-line treatment in certain ABSSSI population, iclaprim's potential advantages over the current standard of care would include demonstrated efficacy with activity against MRSA, no requirement for dosage adjustment, improved safety profile, and potential for shorter treatment duration and hospital stay.

It's currently estimated that roughly 900,000 patients hospitalized in the U.S. with ABSSSI each year have impaired kidneys. Many also present with co-existing diabetes.

Iclaprim is especially suited to this population. It has demonstrated safety in hospitalized ABSSSI patients with kidney impairment and co-existing diabetes.

The ABSSSI patient pool is expanding, driven by the growing prevalence of diabetes and high blood pressure, the two main causes of renal impairment.

Two Additional Indications

A Phase 3 protocol has been finalized for iclaprim in hospital-acquired bacterial pneumonia, including ventilator-associated bacterial pneumonia.

Iclaprim has been shown in a healthy volunteer study to dramatically concentrate in lung tissue following intravenous administration. Efficacy has been demonstrated in a Phase 2 trial in patients with HABP. The addressable market is estimated at roughly $1.7 billion in the U.S.

A potential third indication for iclaprim is MRSA lung infections in cystic fibrosis patients. The first published data on iclaprim's performance in an animal model that mimics the situation in patients with cystic fibrosis were presented 4Q17 at ID Week.

Summary Points

- **In October 2017 Motif Bio reported positive top line results from its second Phase 3 trial of iclaprim, a well differentiated, novel antibiotic candidate for people with serious and life-threatening acute bacterial skin and skin structure infections (ABSSSI).**
- **In both Phase 3 trials, iclaprim achieved the primary endpoint of non-inferiority to vancomycin. Iclaprim was well-tolerated.**
- **Pre-commercial activities are under way for the planned U.S. market launch of iclaprim in ABSSSIs in the first half of 2019.**
- **Motif Bio intends to expand iclaprim's franchise beyond ABSSSI.**
- **A Phase 3 trial is planned in hospital-acquired bacterial pneumonia, including ventilator-associated bacterial pneumonia, where iclaprim's affinity for lung tissue, together with positive Phase 2 results in patients with HABP suggest a high probability of success.**
- **Motif Bio believes iclaprim may also be effective in MRSA lung infections in patients with cystic fibrosis. New data presented 4Q17 showed encouraging results from an animal model that mimics the situation in patients with CF.**
- **The relative scarcity of new antibiotics in the past several decades presents an unusual opportunity for investors in Motif Bio. Several hospital antibiotics (daptomycin, linezolid, levofloxacin) have achieved peak year revenue of more than $1 billion.**

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