



5 September 2018

**Motif Bio plc**  
("Motif Bio" or the "Company")

### **Motif Bio Presents Iclaprim Data at ESCMID/ASM Conference**

- Iclaprim overview presented in State of the Art Lecture
- Safety analysis of diabetic patients in REVIVE ABSSSI trials shows fewer adverse events versus vancomycin
- Surveillance data confirm *in vitro* activity of iclaprim against wide variety of Gram-positive bacteria, including drug-resistant strains

Motif Bio plc (AIM/NASDAQ: MTFB), a clinical-stage biopharmaceutical company specialising in developing novel antibiotics, today announced that iclaprim data are being 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 being held in Lisbon, Portugal, September 4-7, 2018.

#### *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 conducted on the pooled data from the REVIVE-1 and REVIVE-2 trials to evaluate the safety of iclaprim compared to vancomycin, the current standard of care, in treating ABSSSI patients with diabetes. Eleven percent (127/1198) of the REVIVE intent-to-treat (ITT) population had diabetes, and renal impairment was common among these patients, 39.2% (22/56) in the iclaprim group and 36.6% (26/71) in the vancomycin group. Overall adverse events in diabetic patients treated with iclaprim (48.2%) were lower compared to vancomycin (52.9%) and there were fewer treatment-related AEs – iclaprim (8.9%) versus vancomycin (15.7%). No patients with diabetes who were treated with iclaprim developed acute kidney injury/increased blood creatinine levels, compared to three diabetic patients in the vancomycin arm. Discontinuation of study drug due to an AE was reported in 3.6% (2/56) of patients with diabetes treated with iclaprim versus 10.0% (7/70) treated with vancomycin.

**Thomas L. Holland, M.D., MSc-GH, Assistant Professor of Medicine, Duke University School of Medicine, said:** *“Diabetes is a risk factor for ABSSSI and for vancomycin-associated acute kidney injury. Patients with diabetes have worse outcomes with increased clinical failures and longer hospitalisations than patients who do not have diabetes. In the pooled REVIVE ITT population, about 11% of patients had diabetes, and more than a third of those with diabetes had renal impairment. These patients may be particularly vulnerable to vancomycin-related side effects, including kidney toxicity. If approved, iclaprim may be an important new option to treat this patient group.”*

Data evaluating the activity of iclaprim in a variety of bacteria, including drug-susceptible versus drug-resistant strains were also presented at the conference. This included:

*Iclaprim Activity Against Clinical Isolates Causing Acute Bacterial Skin and Skin Structure Infections (ABSSSI) in the Phase 3 REVIVE-1 and REVIVE-2 Studies:* An evaluation of the activity of iclaprim against clinical isolates causing ABSSSI in the REVIVE trials, demonstrating that iclaprim had potent *in vitro* activity against *S. aureus*, including MRSA.

*Surveillance of Iclaprim Activity: In Vitro Susceptibility of Drug-Susceptible and Resistant Beta-hemolytic Streptococci Collected During 2012-2016 from Skin and Skin Structure Infections:* An evaluation of iclaprim against both drug-susceptible and drug-resistant strains of *S. pyogenes* and *S. agalactiae* (samples from patients with ABSSSI collected worldwide during 2012-2016). Data showing iclaprim’s activity had previously

been from samples collected prior to 2006. Iclaprim was shown to be active *in vitro* against these newer strains.

*Surveillance of Iclaprim Activity: In Vitro Susceptibility of Gram-Positive Skin and Skin Structure Pathogens Collected During 2004-2016:* An evaluation of iclaprim against Gram-positive clinical isolates, including *S. aureus* (MSSA and MRSA) and beta-hemolytic streptococci collected from patients with ABSSSI between 2004 and 2016. Iclaprim had consistent *in vitro* activity against these isolates and was shown to be more potent than trimethoprim alone and equally potent compared to trimethoprim-sulfamethoxazole. Iclaprim also had greater potency than standard of care Gram-positive antibiotics such as vancomycin, linezolid and daptomycin against MRSA.

Additionally, David Huang, MD, Chief Medical Officer of Motif Bio, is giving a presentation on iclaprim as part of the **State of the Art Lecture: New Antibacterial Agents**. In his presentation, Dr. Huang provides an overview of iclaprim data in ABSSSI. A New Drug Application for iclaprim in the treatment of ABSSSI is currently under review at the U.S. Food and Drug Administration (FDA) with a target action date under the Prescription Drug User Fee Act (PDUFA) of February 13, 2019.

**Dr. Huang said:** *“Given the worldwide crisis in antibiotic resistance, there remains a major need for new antibiotic treatments. We have shown comprehensive data indicating that iclaprim has potent activity against a wide variety of Gram-positive bacteria, including MRSA, that cause severe skin infections. With its targeted Gram-positive spectrum of activity, low propensity for resistance development, favourable tolerability profile and efficacy results, we think that, if approved, iclaprim could be an important new treatment option for patients with ABSSSI, Including patients with co-morbidities such as diabetes, renal impairment and obesity.”*

The posters and presentation will be available in the Development Programs – Publications section of Motif Bio’s website.

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**Note to Editors:**

## About Iclaprim

Iclaprim is a novel investigational antibiotic with a targeted Gram-positive spectrum of activity. In contrast to commonly used broad-spectrum antibiotics, this “precision medicine approach” is consistent with antibiotic stewardship principles which, among other things, seek to reduce the inappropriate use of broad-spectrum products to avoid the build-up of resistance and to lessen the impact on the microbiome of the patient.

Iclaprim has a different and underutilised mechanism of action compared to most other antibiotics. Following positive results from two Phase 3 trials (REVIVE-1 and REVIVE-2), a New Drug Application (NDA) was submitted to the U.S. Food & Drug Administration (FDA) for the treatment of acute bacterial skin and skin structure infections (ABSSSI) and is now under review, with a PDUFA date of February 13, 2019. To date, iclaprim has been studied in over 1,400 patients and healthy volunteers. Clinical and microbiological data indicate that iclaprim has a targeted Gram-positive spectrum of activity, low propensity for resistance development and favourable tolerability profile. In the REVIVE clinical studies, iclaprim has been administered intravenously at a fixed dose with no dosage adjustment required in patients with renal impairment or in obese patients. The iclaprim fixed dose may, if approved, help reduce the resources required in hospitals since dosage adjustment by health care professionals is avoided and overall hospital treatment costs may be lower, especially in patients with renal impairment. Many standard of care Gram-positive antibiotics are not suitable for hospitalised ABSSSI patients with renal impairment due to efficacy and/or safety issues.

## About Motif Bio

Motif Bio plc (AIM/NASDAQ: MTFB) is a clinical-stage biopharmaceutical company focused on developing novel antibiotics for hospitalised patients and designed to be effective against serious and life-threatening infections caused by multi-drug resistant Gram-positive bacteria, including MRSA. The Company’s lead product candidate is iclaprim. Following positive results from two Phase 3 trials (REVIVE-1 and REVIVE-2), a New Drug Application (NDA) was submitted to the U.S. Food & Drug Administration (FDA) for the treatment of acute bacterial skin and skin structure infections (ABSSSI) and is now under review, with a PDUFA date of February 13, 2019. More than 3.6 million patients with ABSSSI are hospitalised annually in the U.S. It is estimated that up to 26% of hospitalized ABSSSI patients have renal impairment.

The Company also plans to develop iclaprim for hospital acquired bacterial pneumonia (HABP), including ventilator associated bacterial pneumonia (VABP), as there is a high unmet need for new therapies in this indication. A Phase 2 trial in patients with HABP has been successfully completed and a Phase 3 trial is being planned. Additionally, iclaprim has been granted orphan drug designation by the FDA for the treatment of *Staphylococcus aureus* lung infections in patients with cystic fibrosis and is in preclinical development for this indication.

Iclaprim has received Qualified Infectious Disease Product (QIDP) designation from the FDA together with Fast Track status for the ABSSSI indication. If approved for the ABSSSI indication, iclaprim will be eligible for 10 years of market exclusivity in the U.S. from the date of first approval, under the Generating Antibiotic Incentives Now Act (the GAIN Act). In Europe, 10 years of market exclusivity is anticipated.

## Forward-Looking Statements

This press release contains forward-looking statements. Words such as “expect,” “believe,” “intend,” “plan,” “continue,” “may,” “will,” “anticipate,” and similar expressions are intended to identify forward-looking statements. Forward-looking statements involve known and unknown risks, uncertainties and other important

factors that may cause Motif Bio's actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Motif Bio believes that these factors include, but are not limited to, (i) the timing, progress and the results of clinical trials for Motif Bio's product candidates, (ii) the timing, scope or likelihood of regulatory filings and approvals for Motif Bio's product candidates, (iii) Motif Bio's ability to successfully commercialise its product candidates, (iv) Motif Bio's ability to effectively market any product candidates that receive regulatory approval, (v) Motif Bio's commercialisation, marketing and manufacturing capabilities and strategy, (vi) Motif Bio's expectation regarding the safety and efficacy of its product candidates, (vii) the potential clinical utility and benefits of Motif Bio's product candidates, (viii) Motif Bio's ability to advance its product candidates through various stages of development, especially through pivotal safety and efficacy trials, (ix) Motif Bio's estimates regarding the potential market opportunity for its product candidates, and (x) the factors discussed in the section entitled "Risk Factors" in Motif Bio's Annual Report on Form 20-F filed with the SEC on April 10, 2018, which is available on the SEC's web site, [www.sec.gov](http://www.sec.gov). Motif Bio undertakes no obligation to update or revise any forward-looking statements.