MetalloBio Limited - Executive Summary

Problem and Solution

Antimicrobial resistance (AMR) is one of the most serious challenges facing modern medicine, with the World Health Organisation (WHO) announcing that a "post-antibiotic era" is a "very real possibility for the 21st century". AMR is already responsible for 1.2 million annual fatalities globally and this figure is expected to rise to 10 million by 2050 causing a £66 trillion loss to the global economy and as a consequence the WHO has highlighted priority pathogens for which novel treatments are urgently needed.

Our solution is to bring a novel, highly-differentiated antimicrobial class to the clinic. The lead series, based on an entirely new inorganic scaffold which is completely unrelated to any existing antibiotics, has comparable activities to clinically available antibiotics, retains this activity on multi-drug resistant strains, has a novel pluri-modal biocidal mechanism, broad-spectrum activity (Gram-negative and Gram-positive), a broad therapeutic window, and a many-log-scale lower onset emergence of resistance.

Market Opportunity

The global antibiotics market is worth $40.7 billion/annum and is projected to reach $55.8 billion/annum by 2023. Initially, MetalloBio will target the urinary tract infection (UTI) market segment, expected to be worth $12.41 billion/annum by 2025. Additionally, MetalloBio will target the respiratory tract infection market expected to reach $35.5 billion/annum by 2027. Given the compounds' broad-spectrum Gram-negative activity, future growth for MetalloBio will be through targeting other infectious diseases

Competition

First-line UTI treatments (amoxicillin, nitrofurantoin, and trimethoprim) are associated with high resistance rates and several are already incapable of treating WHO priority pathogens. Last-line treatments, including vancomycin, are associated with severe side effects and resistance rates are rising.

In 2020 the global clinical pipeline contained 78 antimicrobial leads. Fewer than 25% of these exhibit the potential to treat WHO and CDC critical pathogens and only 2 represent a new antibiotic class. Of the latter two compounds, gepotidacin targets UTIs; however, it is not active against the majority of Gram-negative priority pathogens, and it only targets uncomplicated UTIs.

Progress to Date

MetalloBio has a proprietary panel of ruthenium-based molecules, and have generated compelling *in vitro* data demonstrating:

- Low minimum inhibitory concentrations (MICs): 1-4 µM against a range of ESKAPE-relevant microbes, including clinical isolates and carbapenem/vancomycin resistant strains
- Low minimum biofilm eradication concentrations (MBEC): <4 µM against a range of ESKAPE-relevant biofilm forming bacteria
- Ultra-low toxicity in mammalian cell lines (IC_{50} at least two orders of magnitude lower than MIC); average therapeutic index of 150; and non-mutagenic to eukaryotic cell DNA
- Little or no signs of toxicity *in* vivo in wax moth larvae (*Galleria mellonella*) across a range of doses (up to 100xMIC [80 mg/kg])
- *In vivo* efficacy: clearance of pathogenic *A. baumannii* infection following a single dose
- *In vitro* DMPK: high microsomal and hepatocyte stability; high plasma protein binding; good CaCO2 permeability
- *In vivo* MTD >30 mg/kg for mono-TMP, >15 mg/kg di-TMP – mouse model
- *In vivo* DMPK: 4.93 hours plasma half-life – mouse model. Efficacy studies ongoing.
- Bioinformatics programme ongoing to optimise the two lead structures
- Multiple mechanisms of action, including a novel intracellular target validated through transcriptomics using RNA-Seq
- Theranostic potential – direct target validation through optical microscopy
- Antimicrobial coating efficacy: biocidal activity in polymeric materials at 1% loading

Intellectual Property Position

A GB patent application was filed in April 2019 – Application No. 1904796.8. A PCT route application was filed in April 2020 – PCT/GB2020/050875 and entered Regional/National Phase for all major territories (including; US, Europe, Asia) in October 2021. In addition, the company owns know-how crucial to the effective handling and manufacturing of the compounds; and has a number of research collaborations with the University of Sheffield from which it will derive valuable data and new IP.

Commercial Strategy

MetalloBio has conducted extensive customer and market engagement by way of Innovate UK's Innovation to Commercialisation of University Research (ICURe) programme. Three commercialisation avenues been identified: antimicrobial drug development (the core programmes); medical device coatings, and materials additives (non-core programmes). Together these promise near-, medium-, and long-term revenue. For the core drug development programmes the strategy is to collaborate/licence with partners in the pharmaceutical sector with the requisite clinical, regulatory, and go-to-market capabilities. Non-core applications are being licensed to specialist players in the med-tech and biomaterials sectors.

Business Model

Drug Development & Partnering

The core patent position is built on broad composition of matter claims supported by considerable inorganic chemistry know-how. It is intended to develop the in-house drug development programmes in readiness to partner at early clinical development (*e.g.* Phase 2a). However, MetalloBio has attracted significant attention already from several major pharma companies with an express interest in potentially partnering before entry to the clinic. The company will assess these overtures on a business case-by-business case basis.

Out-licensing

The full scope of MetalloBio's IP position is being exploited through an active application-specific out-licensing campaign of commercial rights in non-core product development areas (such as med-tech [catheters; intubation tubes] and functionalised materials [textiles; coatings]).

Revenue

MetalloBio closed a Collaboration and Option Agreement with a global specialist portfolio company in Q2 2022. This arrangement will deliver early non-dilutive revenue, with the potential for a full licence agreement to be executed by Q4 2022. All licence deals will include upfront fees, milestone-based payments, and percentage royalties, structured according to expected product development cycles for, respectively, non-medical materials (1-3 years), medical device components (3-7 years), and for pharmaceutical drugs (10-12 years).

Finance Model

To date MetalloBio have been funded by Innovate UK and Royal Academy of Engineering non-dilutive grant funding. A pre-series A fundraising round (target £1.8M) is now open with a lead investor who will commit half the funds, already secured. The proceeds will be used to fund essential preclinical studies to take the lead drug development programme to IND. Follow-on Series A (target £3-5M) and Series B (£5-10M) rounds are expected to follow, aimed at achieving entry to the clinic and further expansion of the team.

The Team

Dr Kirsty Smitten, Chief Executive Officer (LinkedIn); Dr Michael Murray, Executive Chairman (LinkedIn); Dr Richard Senior, Chief Operating Officer (LinkedIn); Ross McMaster, Chief Financial Officer (LinkedIn); Professor Jim Thomas, Chief Scientific Advisor (LinkedIn).

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