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Karl Herz
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Committee Secretary
Senate Foreign Affairs, Defence and Trade References Committee
PO Box 6100
Parliament House
Canberra, ACT 2600
Australia

RE: Submission for Senate Inquiry on the Use of the Quinoline anti-malarial drugs Mefloquine and Tafenoquine in the Australian Defence Force

Biocelect Pty Ltd (Biocelect) is a small private Australian pharmaceutical company, which is currently the license holder from 60 Degrees Pharmaceuticals (60P), and Sponsor with the Therapeutics Goods Administration (TGA) to distribute Tafenoquine in Australia for prophylaxis (prevention) of malaria. The company is also the license holder for Tafenoquine in New Zealand, Papua New Guinea and the Pacific Islands for prevention of malaria. We note that another company – GlaxoSmithKline (GSK) - is the Tafenoquine license holder in Australia (and elsewhere) for treatment of patients with *Plasmodium vivax* malaria.

Biocelect's mission is to identify medicines not currently available in Australia that address an unmet medical need, with the intention of launching them locally. In particular, Biocelect seeks to in-license niche medicines that may not be commercially attractive to the major pharmaceutical companies. If Biocelect is successful in obtaining marketing approval from the TGA for the prevention of malaria, Tafenoquine will be the first product in Biocelect's portfolio. In doing so it will not only address an important medical need within Australia and the surrounding S.E. Pacific Region, but also provide a foundational capability for Biocelect to grow and support future employment within Australia. Biocelect is a 50% female owned Australian SME and the capital to support the registration and commercialization of Tafenoquine has been provided by four Australian families that are shareholders.

Biocelect obtained the license for Tafenoquine from 60P in 2016, and was not involved in any of the original clinical trials on the product. 60P and the US Army have already made significant investment in Australia through creation of a local subsidiary which has engaged local businesses to conduct clinical studies and provide regulatory and commercialisation services.

Our company strongly believes that Tafenoquine is an important addition to the armamentarium now available to combat malaria. Approximately 10.7 million Australians travel overseas each year and it is estimated that approximately 30% of these travel into malaria-prone regions. The current treatments do not provide the full protection needed, either because they do not target all forms of the disease, or because travelers do not adhere to their medicine regimen. Tafenoquine could significantly address both these deficits. Firstly, it is broad spectrum and targets all species of the malaria parasite (including the dormant liver stage of Plasmodium vivax, of which Primaquine and Tafenoquine are the only medications that kill this stage of the malaria parasite lifecycle). Secondly, it has convenient dosing which is weekly, unlike other products that are predominately daily, with the added benefit of one dose on return from the malaria region rather than up to a month of daily medication on return.

We believe it is important for this Inquiry that the use of the term “quinoline” antimalarial drugs can be misleading. While Mefloquine and Tafenoquine are known as “quinoline” antimalarial drugs, they have very different pharmacokinetics, mechanisms of action on the malaria parasite, and very different chemical structures. Mefloquine is a chiral quinoline methanol, while Tafenoquine is an 8-aminoquinoline compound. Hence, one cannot deduce that the safety, efficacy, actions within the body and side effect profile of one molecule from the other molecule.

To date Biocelect has received widespread positive feedback, overwhelming support and encouragement in its endeavors to make Tafenoquine available in Australia for its use in malaria prevention. This support has been primarily from the medical community, ranging from primary care providers, travel health physicians, medical academics involved in malaria and to other interested parties that require products for malaria prevention to provide to their employees that travel to malaria endemic countries.

We are aware of a small group of veterans and their supporters who attribute their mental health issues to having been given Tafenoquine in trials conducted within the Australian Defence Force during their deployment in East Timor. We wholeheartedly sympathise with these veterans and while we recognize and appreciate that they have served our country, based on the evidence available we do not attribute these mental health issues experienced by the veterans to Tafenoquine. We are aware that 60P will be providing information in their submission to this inquiry outlining the science and evidence to support this position. We believe that this position has been confirmed by the recent approval for Tafenoquine as a treatment (radical cure) for malaria by the U.S. Food and Drug Administration (FDA) and the recent recommendation by the U.S. FDA expert Advisory Committee for the approval of Tafenoquine for the prevention of malaria. This recent FDA approval for treatment and FDA expert Advisory Committee recommendation, for approval by the FDA for prevention, was conducted by highly qualified scientific and medical experts based on their review of the scientific evidence. The TGA is also currently reviewing our marketing authorization application with a decision expected very soon.

The foundation of the regulation of therapeutics in Australia and other developed countries is evidence based medicine. It is understandable that some veterans may feel strongly that the issues they face relate to a drug they have taken, especially when provided with ostensibly scientific reasons for their beliefs from people who claim an expertise. However, we have confidence that experienced regulators have the ability to make evidence based judgements, and it is important that they be allowed to do so.

An important part of the regulation of medicines is pharmacovigilance. This means that when a patient reports an adverse event during or after therapy with a drug, that the report is properly investigated, documented and adjudicated by a medical expert on whether it was related to the drug, or from another cause. Recently the TGA, in response to an FOI request, released a summary of 21 anecdotal reports of neuropsychiatric events in Australia. These reports were submitted by veterans or their supporters, who allege that they were caused by Tafenoquine administration in the ADF clinical trials 15 or more years earlier. The reports, the majority of which were reported in 2017, describe events that occurred during and/or many years after the studies were completed. For 17 of these cases for which our partner 60P was able to obtain detailed case information, it was possible to match the line listings in the Sponsor's safety database to specific adverse event reports. In 60P's recent advisory committee briefing document for FDA, they reported the results of this analysis of these cases. In all instances but one, these accounts of adverse events could not be verified as actually having occurred. The other company that has the rights globally for Tafenoquine from the US Army for the treatment of malaria, the multinational pharmaceutical company GSK, reached largely the same conclusion. The FDA also came to this finding, in an independent audit of the Australian Defence Force (ADF) records of the trials the veterans were involved in. For events alleged to have occurred during or after 2017, it is not scientifically plausible based on the available evidence that Tafenoquine could have been a causative factor. It is implausible for Tafenoquine to cause long term psychiatric events if (i) there is no drug in the patient's system when the events occur and (ii) it does not cause meaningful increases in the risk of psychiatric adverse events compared to placebo over the shorter term following administration of drug when drug levels are at their highest. In other words you would need an initial psychiatric event to plausibly claim a later psychiatric event was related. Therefore, with the greatest respect to the veterans affected, their adverse experiences cannot, in 60P's view, be reasonably attributed to Tafenoquine. Biocelect supports the position of 60P in this matter.

If Biocelect is successful in obtaining marketing approval for Tafenoquine from the TGA it is required to undertake the obligation for post marketing / product vigilance on TQ's use, including capturing all reported side effects and reporting these to the TGA. We are committed to this process and believe it is important to continually ensure medicines are having the intended positive outcomes in practice. Biocelect will also provide medical support to experts in the field of medicine and malaria, to ensure they have the depth of knowledge needed to appropriately use Tafenoquine in the right patient.

While it may seem removed from the everyday experience of Australians, malaria is a serious health issue that can even lead to death. Many Australians, including current serving members of the ADF, are exposed to malaria infection every year through travel. Our region also bears a very significant health burden from the disease, and we applaud the Australian Government's initiative to eliminate the disease among our near neighbours. Current treatments do not provide all the answers needed to address this deadly disease, and we strongly believe Tafenoquine meets an important need.

If requested, I would be pleased to appear before the Committee in person to answer questions.

Thank you for the opportunity to express the perspective of one of the Sponsor's on this Inquiry.

With best regards,

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Managing Director
Biocelect Pty Ltd