[redacted]

NABIXIMOLS Rescheduling Application: Applicant's Response to Interim Decision

The Sponsor of the only currently ARTG-Registered NABIXIMOLS prescription medicine [redacted] respectfully acknowledges the Interim Decision of the ACSM dated 7 Feb 2019, but nevertheless continues to defend both changes proposed in its original Application.

The Sponsor maintains its position, and believes it has presented the best international and Australian evidence available to strongly support both:

- Down scheduling of **NABIXIMOLS *as contained in the only ARTG-Registered prescription medicine*** from SUSMP Schedule 8 CONTROLLED DRUG to Schedule 4 PRESCRIPTION ONLY MEDICINE; *and*
- Removal of NABIXIMOLS from SUSMP Appendix D (ADDITIONAL CONTROLS)

Regulatory Controls & Signals of Risk

The Sponsor acknowledges the Committee's concerns which may centre around regulatory control of unregistered cannabinoid products categorised as NABIXIMOLS and their potential for abuse liability, dependence and diversion for illicit use - but re-iterates that the proposed change is *specifically only applicable to NABIXIMOLS as contained in **ARTG (i.e. TGA) Registered** prescription medicine.* This means that all the attendant regulatory controls of a registered prescription medicine apply now, and would continue to apply regardless of whether it is down scheduled to S4 or removed from Appendix D – i.e.:

- Supplied only through a registered pharmacy under a medical practitioner's prescription for the specific TGA-approved indication of spasticity in Multiple Sclerosis once established as a responder;
- Maintenance of current TGA Marketing Authorisation conditions on the ARTG as to the product's ongoing safety and efficacy;
- Ongoing monitoring and oversight of safety signals through the TGA-Approved Risk Management Plan and Australian Specific Annex as part of the Marketing Authorisation held by the Sponsor and Registered by the TGA;
- Periodic Safety Update Reports monitored by the TGA are also required to be submitted by the Sponsor through the TGA-approved Marketing Authorisation Conditions of Registration.

The Sponsor also presented in its Application important and significant evidence that NABIXIMOLS, as available in its registered prescription only medicine [redacted], demonstrates in over 82,000 patient exposure years of post-marketing experience internationally and within Australia that [redacted] as a NABIXIMOLS registered medicine is not associated with problems of abuse, dependence or diversion. [redacted] is a prescription only medicine and is scheduled in major European countries and in wider global countries similarly to the Australian SUSMP Schedule 4 proposed.

[redacted]

Scheduling Policy Framework and Changes to The UN 1961 Convention on Narcotic Drugs

The Sponsor also acknowledges the Committee's second main concern regarding reference to the Scheduling Policy Framework which requires Schedule 8 classification for any substances mentioned in the UN 1961 Convention on Narcotics in Schedules I or II.

The Sponsor, however, urgently draws to the Committee's attention important new UN Recommendation 5.6 which has emerged in respect of this very Convention and changing the classification of cannabis-containing registered pharmaceutical products such as specifically nominated [redacted] out of the UN Convention Schedule I to down schedule into the far less restrictive UN Convention Schedule III. Refer to the Attached Annex 1, Section 5.6, "Extract from the Report of the 41st Expert Committee on Drug Dependence: Cannabis and cannabis-related substances." The extract of the actual Recommendation is as follows:

> ***"Recommendation 5.6:*** *The Committee recommended that preparations containing delta-9-tetrahydrocannabinol (dronabinol), produced either by chemical synthesis or as a preparation of cannabis, that are compounded as pharmaceutical preparations with one or more other ingredients and in such a way that delta-9-tetrahydrocannabinol (dronabinol) cannot be recovered by readily available means or in a yield which would constitute a risk to public health, be added to Schedule III of the 1961 Convention on Narcotic Drugs."*

This means that should this UN Recommendation 5.6 be adopted in due course, then the retention of NABIXIMOLS ([redacted]) in Schedule S8 would not be justified according to the existing Scheduling Policy Framework.

Balance of Risk

The Sponsor therefore believes that on the balance of risks, the benefit to those limited numbers of Australian patients in medical need of a prescription medicine containing NABIXIMOLS such as [redacted], is far outweighed by the perceived risks intended to be controlled by retaining this specific pharmaceutical product on S8 and Appendix D. Further, the UN Convention relevant is in-process for being changed to classify this specific pharmaceutical product into Schedule III of that Convention, thereby removing the requirement for its presence on the SUSMP Schedule 8 according to the Scheduling Policy Framework.

The Sponsor therefore requests reconsideration of the Interim Decision in light of the above clarification and the new UN Convention developments, and if necessary, a deferral of the final Decision until such time as the UN Convention changes are ratified.

[redacted]

5.6 Pharmaceutical preparations of cannabis and dronabinol (*delta*-9-tetrahydrocannabinol)

There are currently two main types of registered medicines that contain *delta*-9-tetrahydrocannabinol (Δ9-THC; dronabinol).

One type is a preparation of cannabis that contains both the psychoactive Δ9-THC and the non-psychoactive cannabidiol in approximately equal concentrations e.g. [redacted]. This is used for the treatment of spasticity due to multiple sclerosis.

A second type contains only Δ9-THC as the active compound and is used for the treatment of anorexia associated with weight loss in patients with Acquired Immune Deficiency Syndrome (AIDS) and for nausea and vomiting associated with cancer chemotherapy in patients who have failed to respond adequately to conventional antiemetic treatments.

Currently approved medicines with Δ9-THC as the only active compound use synthetically produced Δ9-THC, e.g. Marinol, Syndros, although it is possible in the future that medicines with equivalent amounts of Δ9-THC could be prepared from cannabis. There is no difference in the therapeutic effects or adverse effects of synthetic Δ9-THC compared to Δ9-THC from the cannabis plant.

These medicines are all taken orally and are approved for use in a number of countries.

The evidence concerning the use of these Δ9-THC containing medicines is that they are not associated with problems of abuse and dependence and they are not diverted for the purpose of non-medical use.

The Committee recognised that such preparations are formulated in a way that they are not likely to be abused and there is no evidence of actual abuse or ill effects to an extent that would justify the current level of control associated with Schedule I of the 1961 Single Convention on Narcotic Drugs for cannabis based preparations such as [redacted] and the level of control associated with Schedule II of the 1971 Convention on Psychotropic Substances, for preparations using synthetic *delta*-9 THC e.g. Marinol and Syndros.

In order not to impede access to these medicines and in reference to Article 3.4 of the 1961 Single Convention on Narcotic Drugs

- ***Recommendation 5.6:*** The Committee recommended that preparations containing *delta*-9-tetrahydrocannabinol (dronabinol), produced either by chemical synthesis or as a preparation of cannabis, that are compounded as pharmaceutical preparations with one or more other ingredients and in such a way that *delta*-9-tetrahydrocannabinol (dronabinol) cannot be

recovered by readily available means or in a yield which would constitute a risk to public health, be added to Schedule III of the 1961 Convention on Narcotic Drugs.