

25th June, 2012

## **AOD9604 Receives GRAS Status**

- **AOD9604 Receives Pivotal GRAS Status Recognition to enter US Market, conditional on publication of our existing safety data**
- **GRAS Status allows AOD9604 to be added to foods, drinks & dietary supplements in the US**
- **Metabolic will now seek to license this opportunity to US-based companies**

Calzada Ltd's ('Calzada') wholly owned subsidiary, Metabolic Pharmaceuticals Pty Ltd ('Metabolic'), is pleased to announce that it has received a conditional GRAS status determination by an expert scientific panel that its peptide, AOD9604, is deemed Generally Recognised As Safe ("GRAS") and can be consumed at total per capita levels of 1 mg per day. This status, once the conditional task has been completed, will enable AOD9604 to be legally and ethically sold as a component in conventional foods and eventually as a dietary supplement in the USA. As such it is exempt from any further pre-market approval requirements of food ingredients.

This determination was made by a panel of appropriately convened US based experts who are qualified by scientific training and experience. The GRAS evaluation is based on scientific procedures including a detailed review of all of the safety data compiled by the company on AOD9604 since 1998. It reflects the intended use of the peptide in foods, and further reflects the GRAS panel's determination based on the accumulated scientific evidence. Full application of GRAS status is conditional on the straightforward task of arranging publication of the previously completed primary safety studies in a peer-reviewed scientific journal. A journal article is already under preparation.

A GRAS status adds significant value to AOD9604 with commercial benefits anticipated through its licensing to companies who wish to use it in food, drink, and later in dietary supplements.

Metabolic's CEO, David Kenley said "Achievement of a self-affirmed conditional GRAS status is a major value creating milestone for AOD9604. This status is only possible due to the profound safety & tolerability track record of AOD9604 resulting from the Company's past >\$50m investment in the peptide. We now plan to license our intellectual property to US-based companies interested in adding a potential weight management capability to their consumer product range. We aim to receive a significant level of royalties on sales of such products, firstly in the US market and then explore the potential in Europe and the rest of the world."

### **Commercialisation Steps**

As previously advised Metabolic has adopted a low cost out-licensing strategy to derive value from AOD9604. Under full GRAS status, AOD9604 can be legally added to foods and drinks in the US market meaning that it can now potentially be licensed to companies marketing those products in the US.

The benefits of deriving value from AOD9604 in this way are:

- GRAS products are faster and cheaper to get to market; and
- The dietary supplement market for fat reduction, health and well-being is large and growing. We will be able to sell into this market after offering AOD9604 as a food ingredient.

With success in the US market, it is then planned to pursue expansion into European OTC markets via a novel food application and possibly via similar paths into the Australian and key Asian markets.

### **Background**

Metabolic contracted GRAS Associates, LLC ([gras-associates.com](http://gras-associates.com)) to undertake an independent safety evaluation of AOD9604 for use as a food ingredient. The purpose of this evaluation was to ascertain whether or not the intended food uses of the peptide can be considered to be GRAS. Attaining GRAS status enables AOD9604 to be legally added to foods and drinks in the US market at the daily level of up to 1 mg per person.

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### **Appendix 1** (*Information sourced from the GRAS Associates website*)

#### **What is GRAS?**

GRAS is an acronym for the phrase Generally Recognized As Safe. The phrase was used in the 1958 Food Additives Amendment to the Federal Food Drug and Cosmetic Act ("FD&C Act") to exempt certain food ingredients from the definition of food additive. Because the amendment gave new power to FDA to clear food additives only if they were safe before they could be sold, Congress did not want FDA to be flooded with petitions asking them to affirm the safety of flour, salt, gelatin, sugar and hundreds of other familiar and commonly used food ingredients.

FDA promptly compiled a list of GRAS substances but acknowledged in the introduction to the list that the list was incomplete. The FDA also published the procedural regulations for GRAS status in 21 CFR 170.35(d) as shown below:

- (d) The food ingredients listed as GRAS in Part 182 of this Chapter or affirmed as GRAS in Part 184 or Sec. 186.1 of this Chapter do not include all substances that are generally recognized as safe for their intended use in food. Because of the large number of substances the intended use of which results or may reasonably be expected to result, directly or indirectly, in their becoming a component or otherwise affecting the characteristics of food, it is impracticable to list all such substances that are GRAS.

### **GRAS Petitions**

In 1970 FDA began a lengthy review of GRAS ingredients that lasted for more than a decade. In 1972 they established guidelines for the submission of GRAS affirmation petitions for new ingredients. Food ingredients affirmed as GRAS are listed in Part 184 of Title 21 of the Code of Federal Regulations. Substances not affirmed in the review are still listed in the remnant of the original GRAS list in Part 182. A partial list of substances considered GRAS for food packaging materials appears in Part 186.

### **GRAS Notifications**

In 1997, in a cost cutting move, FDA abandoned the GRAS affirmation petition process and proposed procedural regulations that allow for the submission of GRAS Notifications. Although the regulations for GRAS notifications are not final, FDA accepts notifications and posts the review on their website. It should be noted that submission of these notifications is not required but is voluntary.

### **GRAS Self-Determinations**

Ingredients for use in foods must undergo pre-market approval by FDA as food additives or, alternatively, the ingredients to be incorporated into foods must be determined to be generally recognised as safe (GRAS). The authority to make GRAS determinations is not restricted to FDA. In fact, GRAS determinations may be provided by experts who are qualified by scientific training and experience to evaluate the safety of food and food ingredients under the intended conditions of use. [It is such an evaluation which Metabolic has obtained from GRAS Associates.]

### **About Calzada Ltd**

Calzada has 100% ownership of PolyNovo Biomaterials Pty Ltd and Metabolic Pharmaceuticals Pty Ltd. The Company is listed on the Australian Securities Exchange (ASX Code CZD).

### **About PolyNovo Biomaterials Pty Ltd**

PolyNovo owns and develops a suite of state of the art biodegradable polymers that have potential applications across numerous medical fields. PolyNovo has licence agreements and alliances with a number of the world's leading medical device companies and also has joint venture arrangements with local experts in the areas of skin repair.

### **About Metabolic Pharmaceuticals Pty Ltd**

Metabolic's major asset is the AOD9604 peptide which has potential applications in the treatment of obesity, bone, cartilage and muscle diseases and repair. AOD9604 is a small 16 amino acid peptide modelled on one active segment of human growth hormone. It has proven excellent safety and tolerability in a total of six human clinical trials involving 925 humans. AOD9604 is being sold in the market as one of the key components of Phosphagenics' cosmetic anti-cellulite cream called BodyShaper™. Metabolic receives royalties from Phosphagenics on worldwide sales of this product and a share of any sub-licensing revenue that may be received.