

Business Overview

Calzada has two wholly owned subsidiaries:

- PolyNovo Biomaterials Pty Ltd, and
- Metabolic Pharmaceuticals Pty Ltd.

PolyNovo owns and develops a suite of state of the art biodegradable polymers (NovoSorb™) with potential applications across a number of medical fields. The company has an internal program aimed at developing a device for the treatment of full thickness burns (NovoSkin™) and several partnerships including a technology license with Smith and Nephew in two orthopedic fields and a joint feasibility study with a major US based medical device company.

Calzada established **Metabolic Pharmaceuticals** to commercialise the company's AOD9604 anti-obesity compound. It is intended that applications aimed at the treatment of obesity and the prevention and treatment of osteoporosis will be investigated. The company has entered a licensing agreement with Phosphagenics Ltd (ASX:POH). to develop a cosmetic cream called BodyShaper for the treatment of cellulite and localised fat reduction. Calzada will receive royalties on sales of this product.

CEO Report

The past few months have been very exciting with several positive developments being announced. I joined Calzada in November last year and have enjoyed working with Laurent Fossaert (CEO PolyNovo), David Kenley (CEO Metabolic) and the team. I am excited about the future for each of these technologies and good progress has been made towards proving the value in each area.

PolyNovo has seen positive results in their burns treatment product in the recent pig studies. These studies demonstrated that the NovoSkin polymer was superior to the current leading burns treatment product in two critical areas; with lower infection rate and less contraction in the wound. In April this year our collaborator, Burn Surgeon Associate Professor John Greenwood, presented these NovoSkin results to the American Burn Association conference before an audience of hundreds of burns professionals that included fellow surgeons, nurses and scientists. His talk was very well received and he received the inaugural Burke/Yannas Prize for his NovoSkin work.

Meanwhile Metabolic has seen renewed interest in AOD9604 through the launch of the BodyShaper cellulite cream by Phosphagenics. This product, which contains our anti-obesity peptide AOD9604, generated significant media and consumer attention on the back of positive results in a clinical study for cellulite control. Calzada will receive

royalties on the sales of this exciting product. We are now looking at other ways to generate value from AOD9604 in the obesity and bone health markets. In February we released the positive results with AOD9604 in a bone mineralisation study in human stem cells, adding to the substantial amount of data that supports AOD9604 potential in bone health. We are now exploring ways to take AOD9604 to market as a dietary supplement in the US and Europe, initially as a weight loss product. We will update you on this over the next 6 months.

We expect an exciting year ahead with several major milestones expected including NovoSkin burns treatment moving into the clinic and Metabolic AOD9604 generating royalties from the BodyShaper cellulite cosmetic. Thanks for your continued support as a shareholder.



Stewart Washer

FORTHCOMING EVENTS

Results from current ISO10993 safety studies of NovoSkin burns product in preparation for pilot human clinical trial

Royalties from sales of Phosphagenics BodyShaper cellulite cream that contains AOD9604

Way forward for AOD9604 to be marketed as a dietary supplement oral formulation for weight loss in US and Europe

Completion of current NovoSorb™ feasibility study with major medical device company

RECENT HIGHLIGHTS

Success of pivotal animal study on NovoSkin burns product demonstrating superiority against current leading treatment

NovoSkin collaborator Burn surgeon Associate Professor John Greenwood awarded prestigious American Burn Association Burke/Yannas prize for his paper on the NovoSkin burns treatment product

Leading medical device company extends feasibility study with PolyNovo's NovoSorb™ for 12 months including US\$400,000 in milestone payments

Allowance of key PolyNovo patent in the USA

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PolyNovo Biomaterials

We are entering a very exciting phase in the development of the business, our burn project is yielding impressive results and we are progressing towards a very important milestone: first human use.

I am also very pleased for our NovoSkin joint venture partner A/Prof John Greenwood AM who received the inaugural Burke/Yannis award for best bioengineering paper at the American Burn Association annual conference in Chicago last April for his work on our dermal substitute BTM. This work also highlights the great potential for NovoSorb in the field of tissue engineering, tissue such as cartilage or breast could be repaired using scaffolds based on our BTM technology

In this newsletter you will find information related to PolyNovo's BTM, a treatment for full thickness burns, and wound healing mechanisms. I hope it will help you understand our treatment strategy and the advantages afforded by our technology

Laurent Fossaert

CEO PolyNovo Biomaterials

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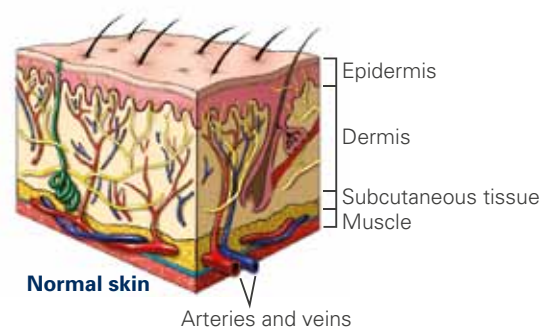
Skin: our largest organ

The skin makes up about 16% of our dry weight and is composed of three distinct layers- Epidermis, Dermis and Hypodermis (sub-cutaneous layer).

Epidermis, the outermost layer of the skin, forms the waterproofing, protective wrap over the body's surface. It is a CELLULAR LAYER. The outer layers of the epidermis consist of dead cells which form keratin as they disintegrate. The epidermis contains no blood vessels with its living cells in the deepest layers being nourished by diffusion of oxygen and nutrients from capillaries in the upper layers of the dermis. The main cells forming the epidermis are keratinocytes. Other cells, with various functions also exist in the epidermis: Melanocytes, Langerhan's cells and Merkel cells. The epidermis constantly regenerates, new cells develop in the deepest (basal) layer, migrate more superficially as they age and change shape and function before dying to form keratin (a process called *keratinisation*). This cycle takes about 27 days. The keratin layer is responsible for maintaining internal hydration and protects against harmful chemicals and pathogens. This mechanical function, together with the immune function of Langerhan's cells, makes the skin a natural barrier to infection. Epidermal loss can be replaced by new cell growth and migration, a REGENERATION process.

The **dermis** is the layer of skin below the epidermis and consists of connective tissue and cushions the body from stress and strain. It is a MOLECULAR LAYER. It is tightly connected to the epidermis by a basement membrane. It harbours many nerve endings that provide the senses of touch (including pain) and heat. It contains hair follicles, sweat glands, sebaceous glands and apocrine glands, as well as lymphatic channels and blood vessels. The blood vessels in the dermis provide oxygen and nourishment to, and waste removal from, its own cells and those of the epidermis. The dermis is responsible for skin's suppleness and elasticity, providing a huge sensory and movement envelope. Because it is a molecular layer, it cannot be regenerated by cellular growth like the epidermis, it can only undergo REPAIR, which results in scar formation.

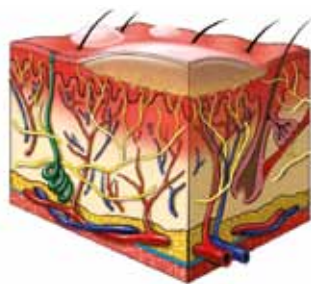
The **hypodermis** (subcutaneous layer) is the layer of tissue situated immediately below the dermis. It consists primarily of loose connective tissue and insulating fat. The larger blood vessels and nerves run within it. The cells within it are fibroblasts, adipose cells (fat cells) and macrophages.



The different types of burns

Superficial partial thickness and mid-dermal burns ('Second degree')

In second degree burns, the epidermis and part of the dermis are damaged. The dead tissues are lost as blister roofs, or are cleaned off in preparation for dressing. These burns will heal spontaneously as long as infection, dehydration, swelling or other insults to the wounds are prevented. Even though the epidermal layer has been lost in the injury, there are 'nests' of epidermal cells in the wound. These cells are surrounding 'epidermal' structures that extend into the dermis (hair follicles, etc.). With loss of the epidermal layer, these cells become reprogrammed. They detach from their basement membrane, divide, and migrate toward and across the wound, initially forming just a single cell layer. This process can be completed in 5-6 days but may take up to 14 days for mid-dermal burns. The more quickly the wound is 'physiologically' closed, the shorter the inflammatory phase of wound healing. It is prolongation of this phase that leads to wound contraction and poor scarring. Burns of this depth can be covered with synthetic membranes to avoid infection and reduce pain.

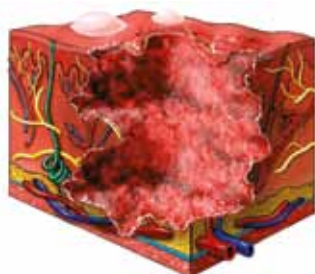


Second degree burn

- Skin blister
- Involves all of epidermis and some of dermis
- May involve all of the dermis

Deep-dermal and full thickness burns ('Third degree')

In third degree burns, all layers are damaged (deep-dermal) or destroyed (full-thickness). The wound bed is either damaged reticular dermis (poor tissue for wound healing) or hypodermal fat. The dead tissue is usually removed surgically (debridement). If left to heal, the only source of epidermal cells for coverage is at the wound margins (all the cell 'nests' mentioned previously have been destroyed in these cases). Additionally, the tissue in the burn base is too poor to allow migration of epidermal cells across it. Two processes occur - the wound bed begins to produce a vascular, collagenous tissue called granulation tissue AND some of the fibroblasts populating this tissue change to become myofibroblasts. These cells can 'pull' on the long, continuous stretches of collagen in the wound to cause contraction. If large wounds are allowed to heal in this way, the resulting scars are appalling and restrict joint movement and general mobility reducing function, cause deformity (especially on the face) and generate significant symptoms (including pain). At the current time, split-skin grafting is used to 'close' the majority of these wounds.



Third degree burn

May extend into deeper tissues

Third degree burn treatment

Autologous (from the same patient) split-skin grafts have been used for extensive wound repair for over a century. They are readily available (in smaller burn injuries), 'free' and do close the wound with tissue from the same individual. Their drawbacks include:

The creation of an extra physiological insult to an injured patient from skin graft donor sites can lead to extremely painful wound(s), which may heal poorly, always leaves a scar in previously uninjured skin and may have very deleterious effects which may prevent mobilisation in elderly patients leading to other complications such as:

- The repair of a deep defect with 'thin' tissue (leading to a degree of wound contraction and lifelong vulnerability of that repair to later thermal, chemical or mechanical insult),
- A repair which is unable to sweat or produce oils to keep itself healthy (these glands, with their epidermal 'nests', are left in the donor site to allow it to heal)

In very large burns (>50% total body surface area), there are insufficient donor sites to allow early closure (allowing the potential for poor scarring) and repeated skin harvest from the same donor sites is often necessary. The use of a dermal substitute to 'temporise' the wound whilst waiting for available skin grafts is employed by surgeons in the developed world - but these materials are too expensive to help burn-injured in poorer countries.



Image: Sid Miller (ABA president) presents the Burke/Yannis prize to A Prof. John Greenwood AM (on the left) at the 43rd American Burn Association meeting in Chicago.

The NovoSkin solution - BTM and CCS: Biodegradable temporising matrix and cultured composite skin for the treatment of deep-dermal and full thickness burns

The classic model of wound healing is divided into sequential, yet overlapping, phases: (1) haemostasis, (2) inflammation, (3) proliferation and (4) remodelling. Upon injury to the skin, a series of complex biochemical events takes place in a closely orchestrated cascade to repair the damage. During this process the patient is highly susceptible to infection and rapid wound closure is of paramount importance.

NovoSkin is developing a two stage treatment for full thickness burns with the ultimate goal of abolishing the need for skin grafts and improving the quality of the resulting tissue and speed of return to function.

How does it work?

BTM is designed to leverage on the beneficial aspects of natural healing, whilst physiologically closing the wound (shortening the phase of inflammation) whilst resisting over-proliferation and wound contraction, discouraging infection and dissolving away when the job is done.

The BTM is placed in the debrided wound, physiologically closing the wound to prevent water loss and creating a barrier to infection. It provides a scaffold for fibroblast migration and proliferation, thus facilitating the different steps that naturally occur during the proliferative phase of wound healing. These include:

- Angiogenesis : new blood vessels are generated to supply nutrients,
- Collagen deposition : new extracellular matrix (ECM) is deposited by fibroblasts.

Wound contraction, which occurs if the deep wound is left untreated, is undesirable and is minimised because the BTM construct 'compartmentalises' the ingrowing tissue, effectively disrupting the formation of long, continuous stretches of collagen which can be manipulated by myofibroblasts (cells which act similarly to smooth muscle cells) to cause contraction. By day 7, the new dermal matrix is integrated and can receive a skin graft.

Novoskin's Composite Cultured Skin "CCS" is the second stage of the strategy, designed to abolish the need for skin graft by producing sufficient quantity of cultured "skin sheets" in bioreactors. A small amount of skin can be harvested from the patient to obtain cells necessary to seed a NovoSorb scaffold; three types of cells are cultured sequentially starting with fibroblasts and microvascular endothelial cells (blood vessel cells), followed by keratinocytes once the scaffold is populated and collagen has been deposited (14 to 21 days). By that time the wound 'temporised' with BTM is ready for grafting. Since the composite skin is "built" using the patient's own cells and the BTM is biocompatible, there is no risk of rejection.

Regulatory path

Medical devices and drugs have different regulatory paths; we are currently working with a regulatory consultant to define PolyNovo's strategy.

Different jurisdictions have different requirements for devices, although the same types of data are used. The key requirements for BTM, an implantable device, are safety and efficacy. Safety studies under ISO10993 are currently underway in Germany and will be completed by the end of the year, those results combined with the multiple animal studies performed to date will be used to seek approval for our first human trial in full thickness burns. To date all the animal studies performed better than expected even when compared to current best practice treatments and are confident we will receive the necessary approval for our first human trial by late 2011.

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Metabolic Pharmaceuticals

AOD9604 – Past, Present & Future

From 1998 to 2007 Calzada invested approximately \$50m into the pre-clinical development of AOD9604 and the completion of 6 human clinical trials. A total of 925 patients were involved in these trials which generated much valuable data. This data is valuable because it :

- shows a clear track record of excellent safety and tolerability;
- revealed some indications of real oral efficacy; and
- offers potential to restart the clinical trial process from the relatively advanced stage of phase 2.

In February 2007 all development of AOD9604 was terminated following completion of a large oral phase 2b human trial which failed to prove efficacy. Possible reasons for this failure include:

- oral delivery of a peptide is very difficult;
- change in drug regimen from capsule to tablet; and
- inclusion of a tough diet and exercise program diluted the drug effect.

Both the inventor (Professor Frank Ng) and current CEO of Metabolic Pharmaceuticals Pty Ltd, Mr David Kenley, viewed this termination as premature as some evidence of efficacy was shown in a subset of women and in the five previous human trials. Calzada decided to reconsider the future of AOD9604 and reinvest in commercialisation of its peptide due to the following two key reasons:

1. Phosphagenics wanted to develop a transdermal cosmetic product centered on AOD9604. This made sense because three of Phosphagenics' key scientists, including the CEO Dr Esra Ogru, had an in depth knowledge of AOD9604 through completion of their PhDs in the inventor's Lab and were employees of the company at the time of its commencement and whilst Calzada operated a laboratory at Monash University. Additionally, Phosphagenics had a proven transdermal delivery technology and a willingness to invest significant funds in the development of a transdermal product.
2. In early 2010 we discovered the 'black market' trade in AOD9604. This revealed over 20 Chinese websites offering AOD for sale at selling prices of up to US\$30,000 per gram. After investigating the sales from China we found that AOD9604 was being bought by distributors, gymnasiums, weight control centres, private clinics and individuals (athletes, bodybuilders and the obese) with delivery via sub-cutaneous injection once or several times per day.

We have found significant anecdotal evidence amongst these users of the effectiveness of AOD9604 in the reduction of trunk fat without side effects except minor soreness around the injection site. Based on detailed market research of the larger Shanghai, China based producers we estimate the total world 'black market' could be up to US\$40m per annum. Recently US based manufacturers have appeared offering AOD9604 for sale for further expanding this illegal market.



In August 2009 Calzada announced that it had signed a collaboration and option agreement with Phosphagenics for a transdermal cosmetic application. In September 2010 Calzada announced the successful negotiation of a license with Phosphagenics for that application.

Phosphagenics have recently launched their new Elixir branded product, titled BodyShaper [refer back page], into the Australian market with Asian, US and European markets to be opened later in 2011. Revenues from royalties and a share of all sub-licensing income will flow to Calzada from sales of the BodyShaper anti-cellulite cream. The potential world market for this product is substantial and sales success increases Calzada's prospects of developing other applications for AOD9604 including pharmaceutical (for obesity and other potential applications such as Osteoporosis) and new OTC / dietary supplement opportunities.

We are determined to realise further significant value for our shareholders in the future from AOD9604. We are doing this by actively investigating alternative delivery methods, dietary supplement and nutraceutical applications and new potential pharmaceutical applications. We aim to achieve significant progress in at least one of these areas within the next 12 months.

David Kenley
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Bodyshaper Cellulite Contour Crème™

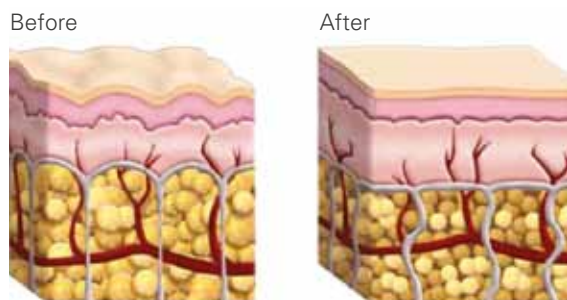
In August 2009 Calzada agreed to collaborate with Phosphagenics Ltd (ASX : POH) to develop a cosmetic cream to deliver AOD9604 into skin using Phosphagenics' TPM transdermal delivery system. By September 2010 the collaboration had yielded positive development progress. Phosphagenics then exercised an option to licence AOD9604 for their transdermally delivered cosmetic applications.



On 11 April 2011, Phosphagenics released positive interim results from a 30 female human trial conducted by AMA Laboratories Inc., based in New York, of their new product containing AOD9604. Further trial data was released by Phosphagenics on 17 May 2011.

This cosmetic product is titled BodyShaper Cellulite Contour Crème™ and was launched under Phosphagenics' Elixia® cosmetics brand on 20 May 2011 in Myer stores. BodyShaper has been developed to assist the body reduce cellulite and subcutaneous fat.

Cellulite describes the appearance of bumpy looking fat on the body. It is not a disease, but a condition where bulging fat cells and other coexisting factors result in the appearance of cellulite.



Before and after cross-section of cellulite

The global market for facial skin firming/tightening/anti-cellulite products was US \$2.8 billion in 2008 and predicted to reach US \$4.8 billion by 2013.

BodyShaper combines AOD9604 with Tricellite Active™ ingredients which are a concentrated blend of antioxidants, moisturisers and patented TPM® delivery technology to give skin a firmer, more toned appearance. The unique Tricellite Active™ combination brings together AOD9604, Forskolin and Caffeine – a trio of fat-reducing ingredients scientifically proven to reduce the size of fat cells. TPM® delivery technology has demonstrated it can improve the delivery of many active ingredients by up to five times during scientific testing.

Future plans

Phosphagenics senior executives continue to build strong relationships with key strategic national and international retailers, who offer specialist business expertise and exposure to consumers at store level that is essential to effectively selling BodyShaper on a worldwide basis. Phosphagenics will also offer BodyShaper for sale directly through their dedicated Elixia® website. **We have arranged with Phosphagenics for Calzada shareholders to receive a 25% discount on BodyShaper products. Please refer to enclosed BodyShaper offer brochure.**

BodyShaper Cellulite Contour Crème™ is also generating substantial interest in international markets which are being explored with discussions ongoing particularly in the South East Asian region and the USA as the first steps in creating global success for our Australian developed product.

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