

17 October 2011

## **Successful Proof of Concept for Synthetic Skin**

Calzada (ASX: CZD) is pleased to announce that the first animal results testing NovoSkin's Cultured Composite Skin (CCS) have been extremely encouraging. Associate Professor John Greenwood will include these findings in his AusBiotech presentation at 3.00pm today. A copy of this presentation is attached.

The CCS forms part of NovoSkin's two stage treatment strategy for full thickness burns aimed at abolishing the need for skin grafts.

The Biodegradable Temporising Matrix (BTM) is the first stage with successful results announced on 3 March 2011. This product is currently scheduled to be tested in a human clinical trial later this year as announced on 4 July 2011.

The CCS is the second stage of the product and is a bi-layer synthetic skin using the patient's own cells and a NovoSorb scaffold. John Greenwood's team was able to successfully produce CCS and implant that product into the animal to create a viable form of skin in a clinically relevant timeframe.

Mr Laurent Fossaert commented: 'Producing tissues in bioreactors is a well established process, however problems frequently occur those bioengineered tissues are implanted in vivo. In this preliminary study we showed that CCS is viable after implantation and does not require an external source of nutrition. This is a very important proof of concept result for our CCS product. Importantly it also opens the potential to utilise this technology in many other tissue engineering opportunities'.

### **For further information please contact:**

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### **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).

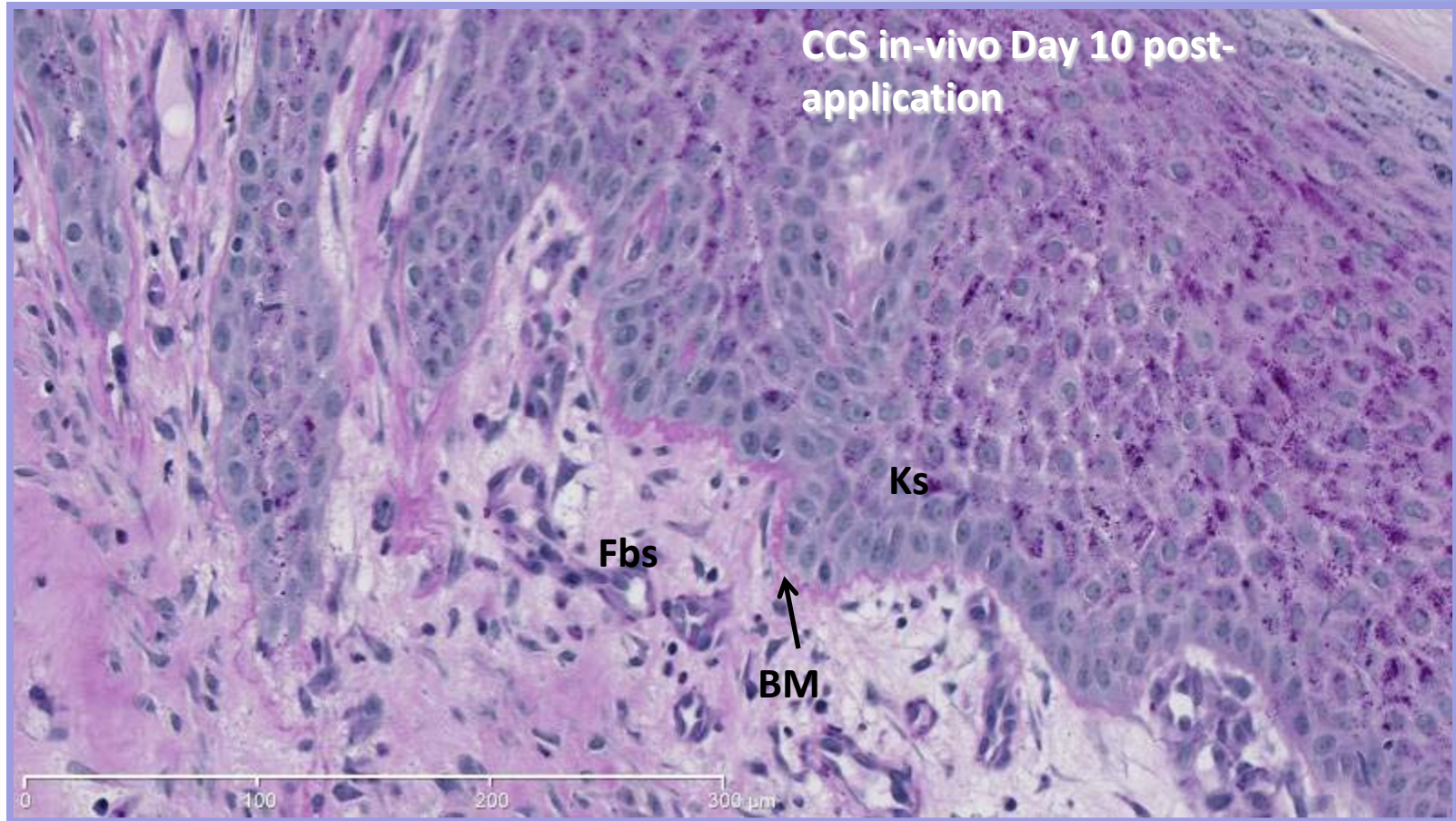
### **About PolyNovo Biomaterials Pty Ltd**

PolyNovo owns and develops a suite of highly prospective biodegradable polymers that have potential applications across numerous medical fields. The group 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 and bone disease. 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. Growth hormone occurs naturally in the body and has profound stimulatory effects on fat metabolism. Levels of the hormone are typically suppressed in the obese state and with increasing age. Counteraction of this imbalance by dosing with AOD9604 is believed to normalise suppressed fat metabolism in obese individuals, while avoiding unwanted effects of the whole growth hormone molecule.

# THE NOVOSKIN PROGRAM



**A/Professor John E Greenwood AM**

BSc(Hons), MBChB, MD, FRCS(Eng), FRCS(Plast), FRACS

Director, Adult Burn Service, Royal Adelaide Hospital, South Australia

Director, Skin Engineering Laboratory, SA Pathology

Director, Novoskin Pty Ltd

# TWO STAGE PROCESS

- BTM

- Applied immediately post-burn excision
- Provide a structure to guide dermal invasion
- Prevent or minimise wound contraction
- Prevent infection
- Reduce pain
- Temporarily 'close' the wound
- Prepare the wound bed for composite

- CCS

- Applied when ready
- Should have ability to definitively 'close' the wound
- Should ideally consist of an autologous collagen matrix produced by fibroblasts, infiltrated by endothelial cell-lined 'vessels', surfaced by keratinocytes anchored by a basement membrane
- Should 'take' onto the prepared BTM

## ❖ ISO 10993 safety studies

### ❖ *In-vitro* studies thus far:

- human skin cell cytotoxicity
- human skin cell mat matrix compatibility
- human skin cell foam matrix compatibility

### ❖ *In-vivo* studies thus far:

- rat implantation safety
- sheep wound engraftment
- pig engraftment; immediate and delayed
- pig comparative; BTM vs Integra<sup>®</sup>
- pig; integrated BTM plus CEA
- Pig; integrated BTM plus CCS

# PRODUCTS

- **IDT** (Immediate Dermal Template)
- **BTM** (Biodegradable Temporising Matrix)
- **CCS** (Cultured Composite Skin)
- **BTM Generations** (Pharmaceutical/Cytokine Elution)
- **CCS Generations** (Vasculature, Adenexae, Pigmentation)

**IDT**

**(Immediate Dermal Template)**

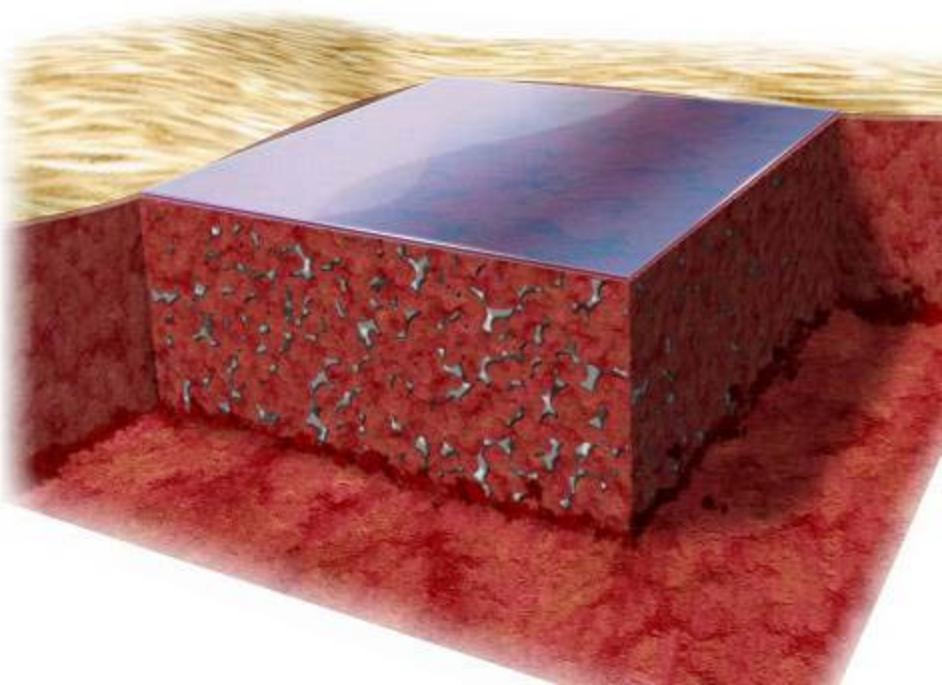
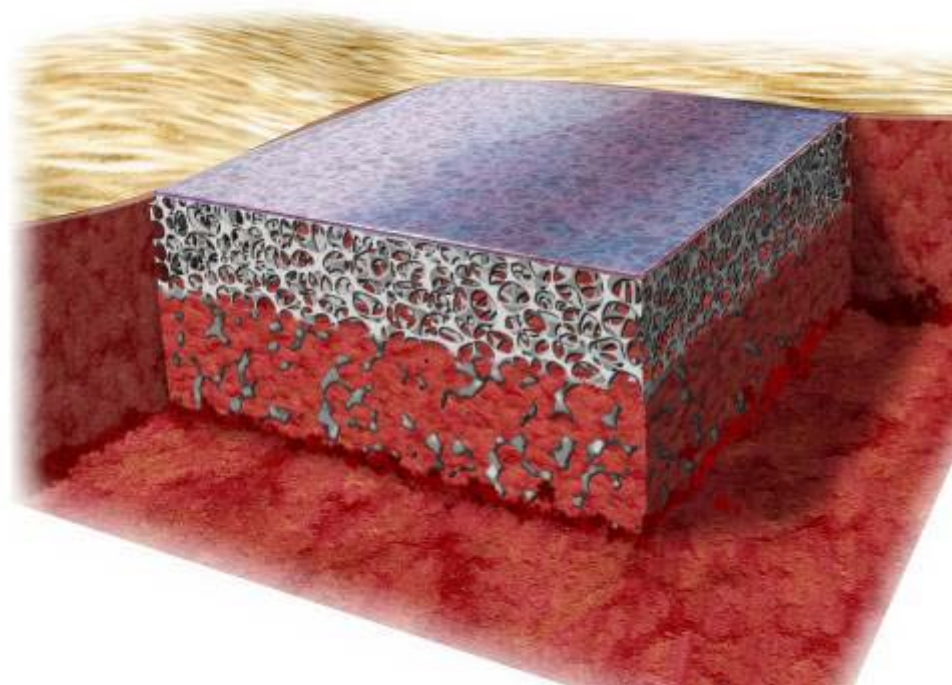
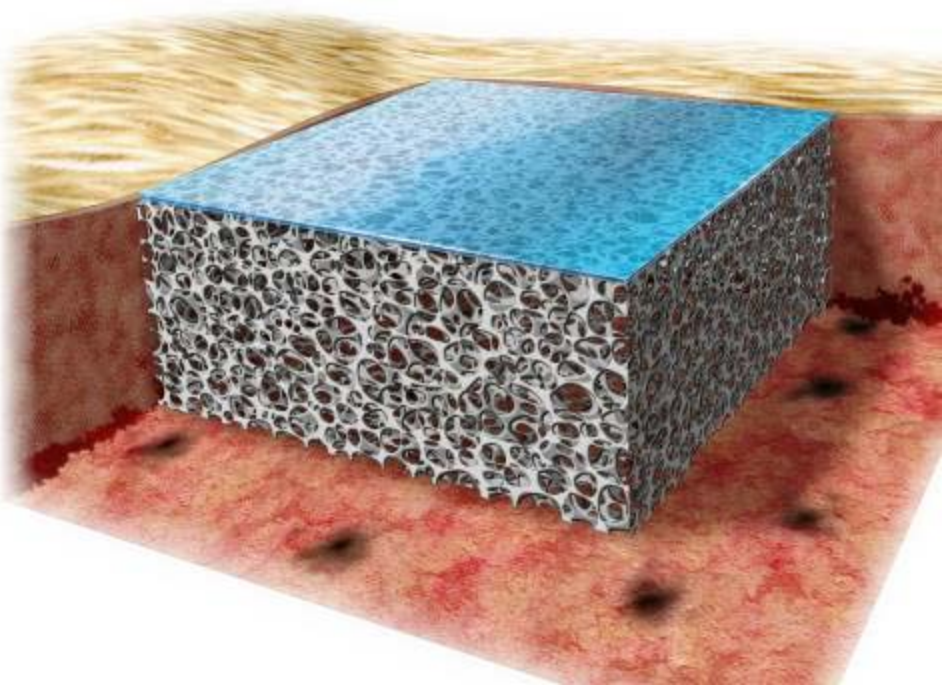




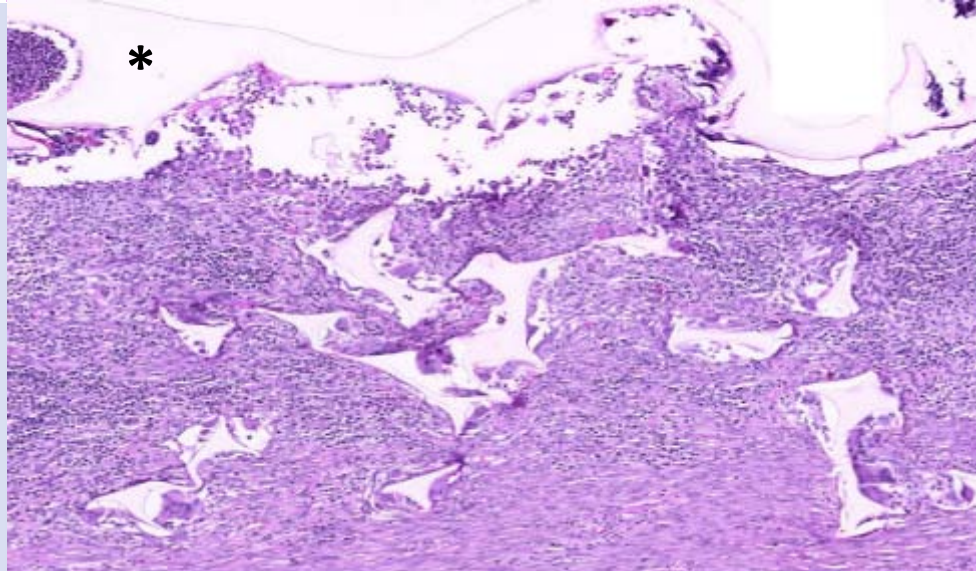
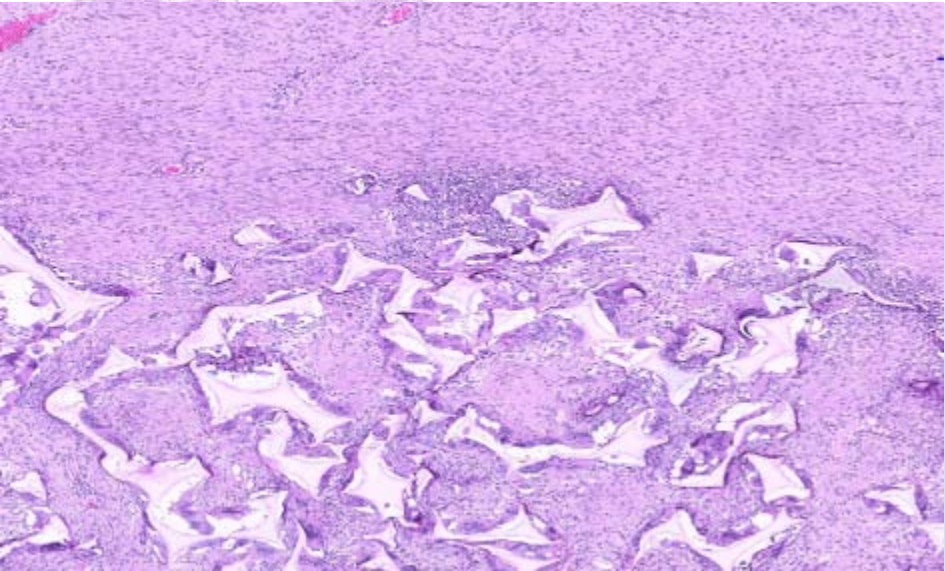
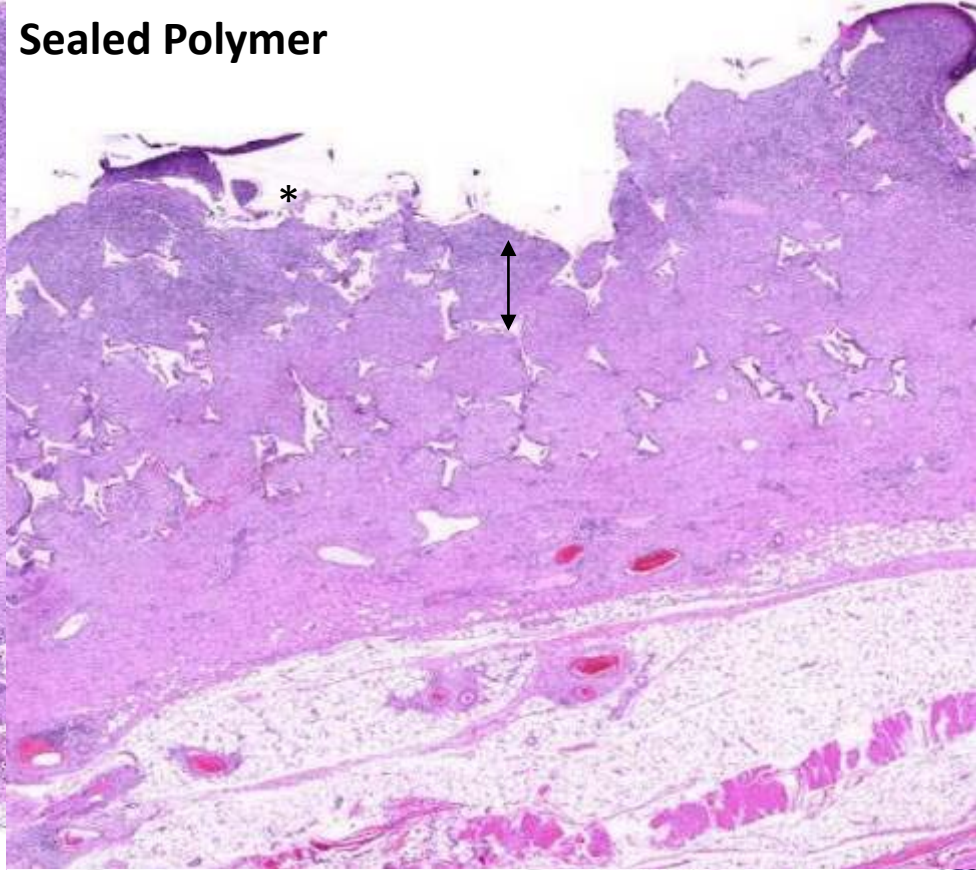
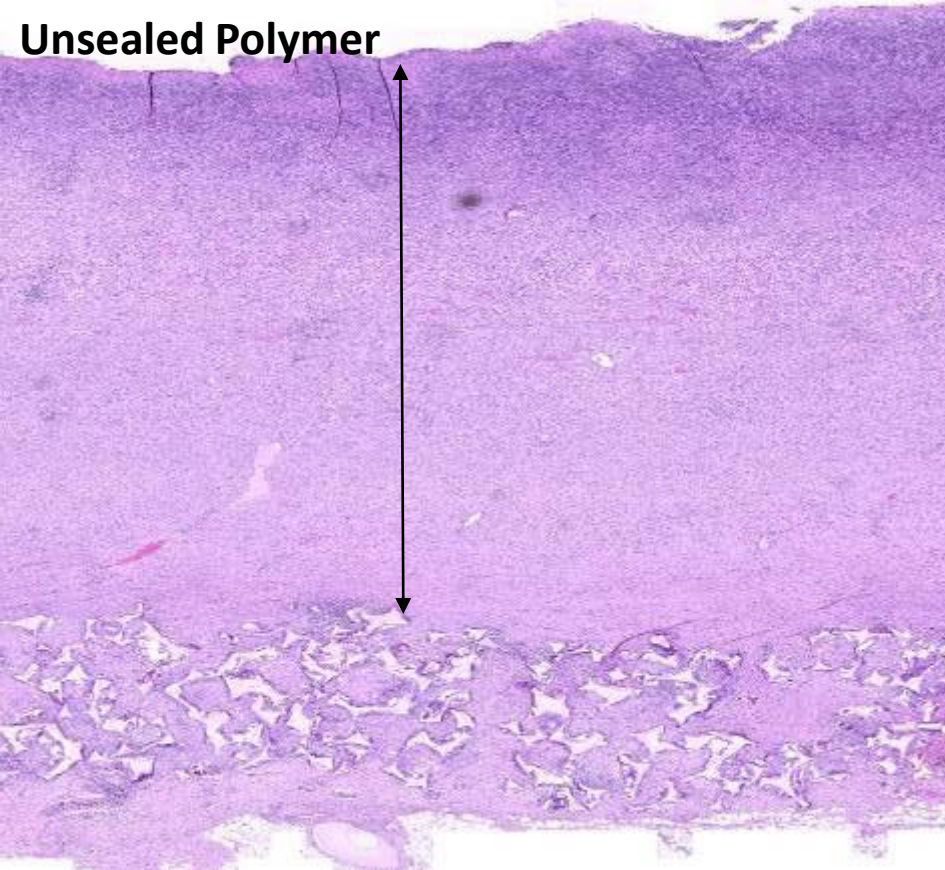
**BTM**

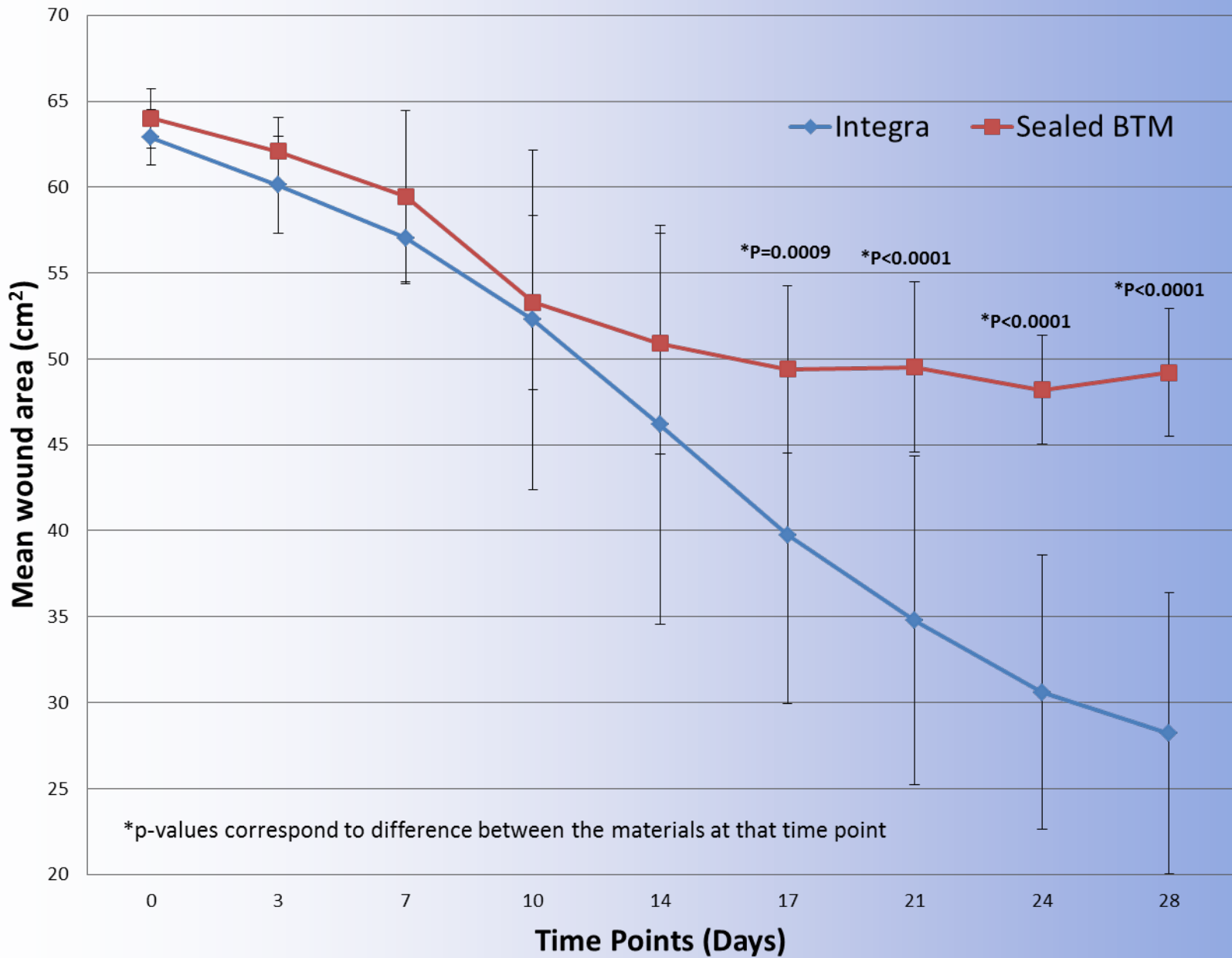
**(Biodegradable Temporising Matrix)**





# INTEGRATION SCHEMATIC





CCS

(Cultured Composite Skin)

# CCS on BTM

*in-vivo*

Keratinocytes

CCS Matrix

Fibroblasts/collagen

BTM Matrix

Subcutaneous fat



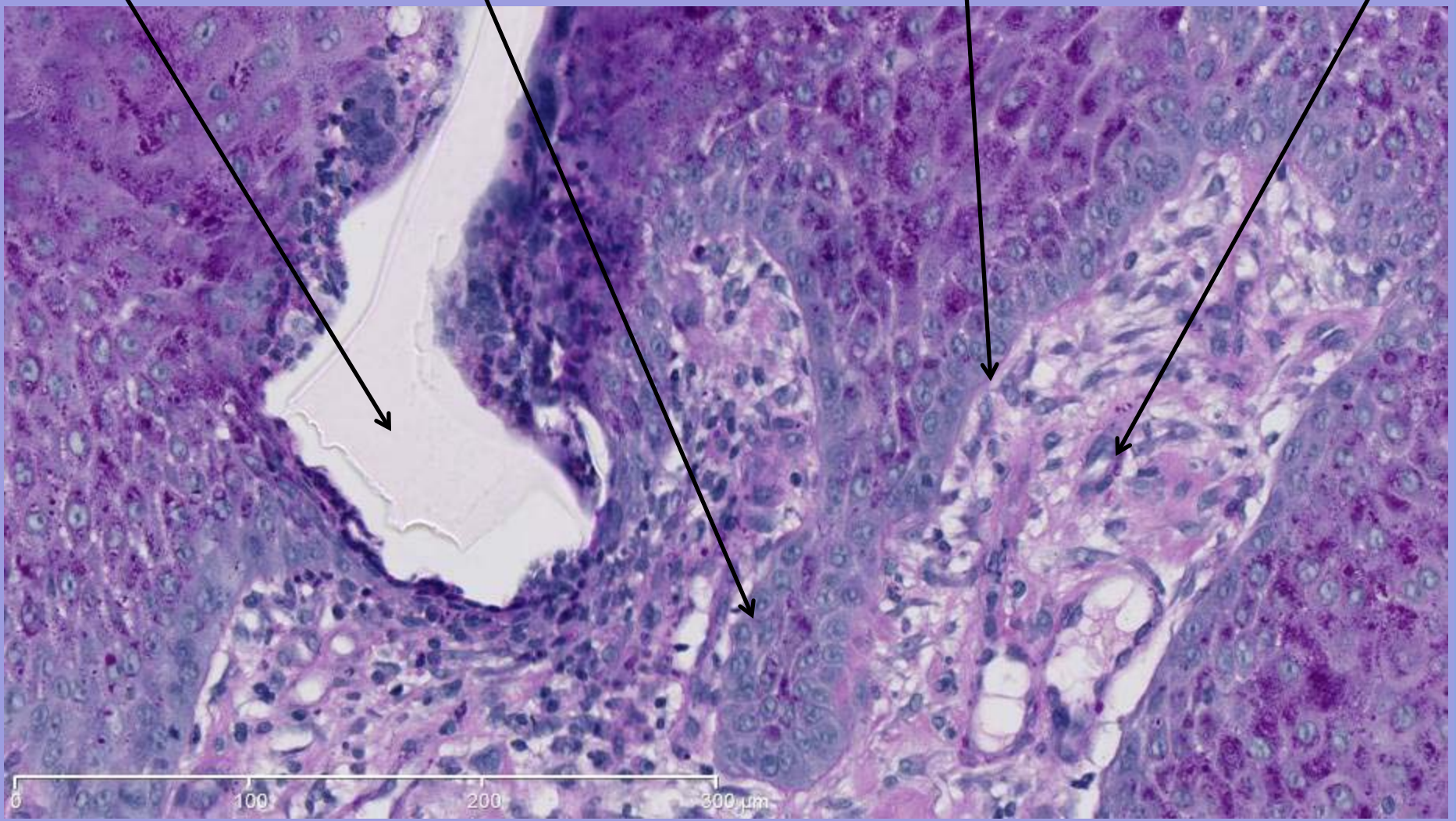
# CCS *in-vivo* (Day 7 post-application)

Polymer matrix

Basal keratinocytes

Basement membrane

Fibroblasts





# SUMMARY

- NovoSkin has a suite of products in development based on the NovoSorb platform, and generational products planned
- Good research evidence of safety of NovoSorb
- Good research evidence of efficacy of IDT and BTM
- Good proof of concept of CCS 'take'
- **THEREFORE - SUCCESSFUL PROOF OF CONCEPT OF THE DESIGNED TWO-STAGE STRATEGY**