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ASX Announcement

NovoSorb BTM delivers positive First in Man results in Cell Therapies

PolyNovo is pleased to announce that Professor Toby Coates AO, Director of Beta Cell Technologies Pty Ltd (Beta Cell) presented to the Joint Congress of ESPE and ESE on 12 May in Copenhagen outlining the results of PolyNovo's NovoSorb's leading role in treating and managing Type 1 diabetes (T1D).

In this proof-of-concept study Professor Coates reported survival and function of human pancreatic islets transplanted into an alternative neovascularised site within the skin using Novosorb BTM to create a cell supporting vascular bed. The trial involved in 3 participants with long-standing Type-1 Diabetes who received islet cells after kidney transplant. (refer to annexure)

Professor Coates said, "Our results are the culmination of the past 10 years of research and development using the NovoSorb technology and islet cells in rats and pigs and now in a "first in human study". For the first time we report both 3-year survival and function of human pancreatic islets transplanted within the NovoSorb BTM site outside of the liver. The results show an exciting new opportunity for the NovoSorb technology in cell therapies as a delivery vehicle."

The current standard of care to treat Type 1 diabetes is to transplant human islet cells into the liver. However, researchers report that 75% of cells are lost in the first 48 hours. Prof Toby Coates AO reports, "The problem with this treatment is that the transplant site cannot be easily biopsied and the islet cells can't be monitored or retrieved so it is difficult to detect and remedy islet rejection."

Professor Coates explained that, "PolyNovo's NovoSorb has some unique properties such as its ability to create a vascular bed capable of supporting the cells and, as the islet grafts are held within the NovoSorb matrix, the cells can be easily located and monitored in vivo. Additionally, the NovoSorb matrix properties enable the use of topical immune suppression which could be potentially 'topped up' easily if needed."

Professor Coates noted, "This week we passed the third anniversary of the first human implant and remarkably the T1D patient's sugar level has remained within a normal range at 5mmol/L with no requirement to top up cells over the journey."

PolyNovo Chairman David Williams said “I have been closely following the research undertaken by Beta Cell at the invitation of Professors Coates and Greenwood (who was instrumental in the invention of NovoSorb BTM) for the last three years. These are very exciting results, and a red-letter day potentially creating a new and distinct silo for the PolyNovo business; one in Wound Care and related uses, and another in Cell Delivery.”

Professor Greenwood, who conceived of NovoSorb BTM, says that, “when I was developing the BTM, I always had a vision that the BTM platform, if successful in burns and wound care, would have the capability to be used in other cell areas. The results of our trials confirms that the NovoSorb technology has the potential to be a game changer in the cell therapy space. As a bonus, we think because BTM and the cells are both approved, there are fewer regulatory hurdles.”

PolyNovo has been supplying the NovoSorb BTM material to Beta Cell at no cost during their product development program and Beta Cell has successfully established and developed collaborations with major cell therapy players such as the global leader in T1D based in Denmark, Breakthrough T1D based in New York, JDRF Australia and the Garvan Institute in Sydney.

Chairman David Williams says, “It goes without saying we are extremely excited about the use of PolyNovo as a delivery device in cell therapies. Professors Coates and Greenwood have articulated the properties of our technology that should make it attractive to other cell therapy companies”.

PolyNovo anticipates that Professor Coates will participate in the shareholder webinar on Friday this week.

Going forward, PolyNovo and Beta Cell are in collaboration discussions to accelerate research and development pathways to ensure PolyNovo’s technology can play a major role in the cell therapy market space which is estimated to be USD $34 Billion by 2034. Professors Coates and Greenwood are subject matter experts and will guide PolyNovo’s involvement.

This announcement has been authorised by PolyNovo Company Secretary, Jan Gielen.

About PolyNovo®

PolyNovo is a disruptive medical technology company, headquartered in Melbourne, Australia. Its products simplify management of acute complex wounds, redefining healing with meaningfully differentiated patient outcomes across multiple wound etiologies. The Company has treated 70,000+ patients in 46 countries and is investing for growth via new products, indications, and markets. For more information see polynovo.com.

About NovoSorb®

NovoSorb BTM is a dermal scaffold for the regeneration of the dermis when lost through extensive surgery, trauma or burn. NovoSorb is a novel range of bio-resorbable polymers that can be produced in many formats including film, fibre, foam, and coatings. NovoSorb’s unique properties provide excellent biocompatibility, control over physical properties, and a programmable bio-resorption profile.

Connecting Endocrinology Across the Life Course
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European Society of Endocrinology

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The Proof of Concept INCEPTR trial 12 month outcomes – Intracutaneous islet transplant in humans into pre-vascularised Novosorb® neodermis.

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Introduction : Allogeneic islet-cell-transplantation (ICT) is an established treatment for hypoglycaemic unawareness for selected people living with Type-1 diabetes (T1D) available in Europe, the UK and Australia. As ICT is currently practiced, allogeneic human islets are transplanted into the liver via the portal vein. However, up to 75% of the transplanted islet mass is lost within the first 48 hours post-transplant, due to the Instant Blood Mediated Inflammatory Reaction. Furthermore, the hepatic transplant site is unable to be easily biopsied, transplanted islets are unable to be monitored or retrieved, limiting the ability to detect and treat islet graft rejection. In order to develop an alternative to intra-hepatic ICT we pre-implanted a Biodegradable Temporizing Matrix (Novosorb®) into the inner-bicep of three trial participants prior to ICT as part of our **IN**tra-**C**utaneous **E**ctopic **P**ancreas **TR**ial – INCEPTR. Pre-implantation of Novosorb® created a fully functional dense vascular bed capable of supporting transplanted islets within the intracutaneous-transplant site (Diabetes 2023 PMID: 36929171). Unlike the hepatic site, intracutaneous islet grafts can be monitored *in vivo*, enable topical immunosuppression and removed in toto, thus creating an attractive site for gene modified, xenogeneic- and stem-cell-derived ICT.

Method: INCEPTR is a prospective first-in-human study of allogeneic ICT into a pre-vascularised intracutaneous transplant site : Australian and New Zealand Clinical Trials Registry (ACTRN12621001573842). The INCEPTR trial primary outcome was detectable c-peptide at 3 months post-transplant. Secondary outcomes included average daily exogenous insulin usage and HbA1c measured at baseline, 3, 6 and 12 months post-transplant.

Results: Three immunosuppressed kidney transplant patients with longstanding T1D (c-peptide negative) underwent Novosorb® implantation under local anaesthesia as outpatients prior to intracutaneous cadaveric human islet transplantation.

Pt	Pre-Islet transplant Novosorb® integration period	Total IEQ transplant	3/12 c-pep	3/12 HbA1c reduction	3/12 insulin Reduction	6/12 HbA1c reduction	6/12 insulin reduction	12/12 HbA1c reduction	12/12 Insulin reduction
1	25 days	485,584	pos	1.1%	21%	1.8%	22%	1.8%	28%
2	33 days	204,633	neg	1.1%	10%	0.6%	7%	0.8%	21%
3	76 days	276,026	pos	0.3%	44%	0.3%	44%	1.3%	62%

Conclusions: In this study two of three participants had positive c-peptide at 3 months with all patients showing improvement in glycaemic control over 12 months. One of the patients with positive c-peptide at 3 months has ongoing long-term detectable graft function out to 2.5 years post engraftment. The prevascularised Novosorb® neo-dermis is safe and supported human islet cell survival in an intracutaneous transplant site outside of the liver.

Disclosure of interest: Patrick Coates Inventor and Shareholder in Beta Cell Technology, Daniella Penko: None declared, Jodie Nitschke: None declared, Julie Johnson: None declared, Svjetlana Kireta: None declared, Elizabeth Concannon: None declared, Tom Loudovaris: None declared, Alice Rickard: None declared, Colleen Etherton: None declared, Patrick Coghlan: None declared, David Torpy: None declared, Thomas Kay: None declared, Shane Grey: None declared, John Greenwood Inventor of BTM technology and shareholder in Beta Cell Technology, Chris Drogemuller: None declared