Newsletter to Medigard Shareholders

Explaining Medigard's New KT009 Program - Injection Treatment of Degenerative Disk Disease (DDD), chronic lower back pain and maybe osteoarthritis (OA)

Key points

- KT009 development program is well defined and aims at clinical study within 3 years
- KT009 product is expected to be safe and biologically active to treat disc disease
- A de-risked product could be partnered

Medigard shareholders have been following the recent announcements of an exclusive worldwide license agreement with Kunovus Pty Ltd under which Medigard will commercialise the patented KT009 injectable product to treat intervertebral disc degeneration (IVDD), debilitating degenerative disk disease (DDD), chronic lower back pain and maybe osteoarthritis (OA).

In this newsletter to shareholders, we seek to explain this program in some more detail.

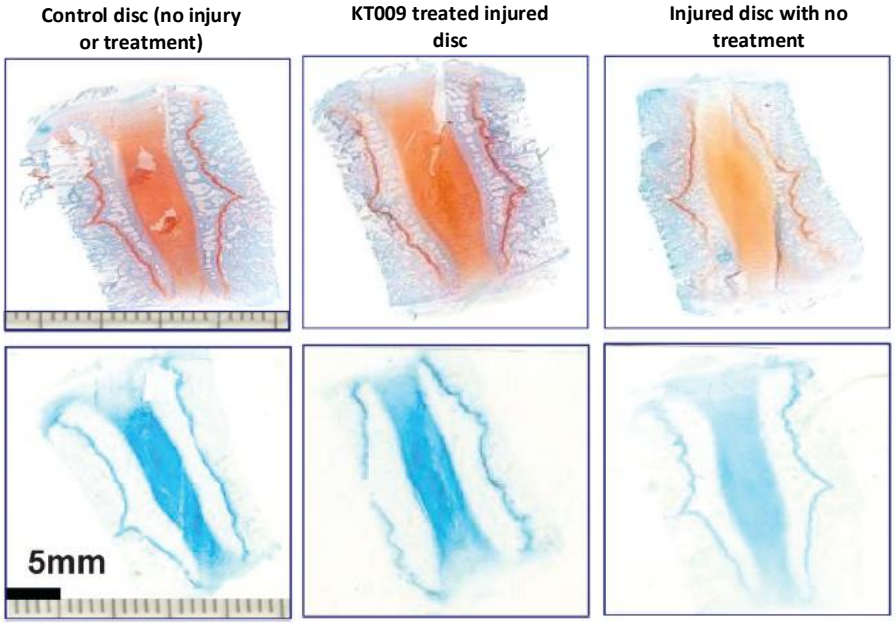
What is the KT009 treatment ?

The treatment will involve a guided injection of KT009 into the disc space in between the two vertebra – using a specialised proprietary injection device. The treatment would likely be conducted as a day procedure by a specialist doctor or at a radiology facility.

Medigard has also negotiated the rights to commercialise other uses of KT009.

What stage is the KT009 program up to ?

The KT009 therapeutic agent (drug) has already undergone non clinical testing in animal models of degenerative disc disease and showed safety (no adverse events) and efficacy [1].

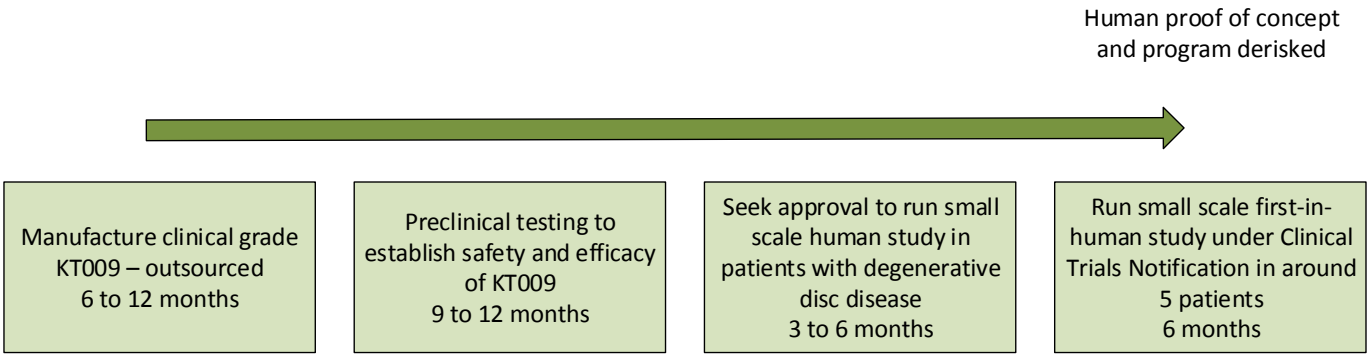


The above pictures show that following an injury to the disc, KT009 treated disc joints (middle panel) are similar to undamaged controls (left panel) and superior to injured disc joints that were not treated (right panel).

[1] Int J Biol Sci. 2009 Jun 3;5(5):388-96.

From here the KT009 development program is actually very well defined :

KT009 Development Program in Australia 24 to 36 months (estimated)



While we have a good idea of overall expenses, we are presently working to better define the cost and timing of the KT009 development program.

Manufacture of KT009 will be outsourced to a credible and experienced Contract Manufacturing Organisation (CMO). Initial clinical studies will be conducted in Australia. Patient response can be imaged readily to give early read-outs of progress.

What is KT009 and why will it treat patients with DDD ?

KT009 is the name given to an injectable *endogenous recombinant protein* GDF-6 (also known as BMP-13 and CDMP2).

In adults, GDF-6 levels decrease with aging, coincident with increased incidence of degenerate disc disease. Cells exposed to GDF-6 have reduced levels of cell death [2] and reduced senescence [3]. Children born with mutations in GDF-6 gene can suffer Klippel-Feil syndrome [4] – a condition where there is incomplete separation of the cervical vertebrae i.e. incomplete formation of the intervertebral disc.

It makes sense that injecting extra KT009 into the disc space could help patients with DDD, if a shortage of GDF-6 is associated with disc degeneration or malformation.

It is worth explaining what an *endogenous recombinant protein* is :

- endogenous means growing or originating from within – i.e. something which is natural to our bodies and naturally normally made by our tissue. Another endogenous protein is insulin – which our bodies make to control blood sugar levels
- recombinant means artificially produced (and often purified) in a biomanufacturing facility – an artificial means to make proteins rather than harvesting them from humans or animals. Injectable insulin, as an example used to be harvested from pigs or cows but is now made as a recombinant protein
- protein means a large molecule that is made of amino acid units – also referred to as biologics. Insulin is around 110 amino acids and KT009 is two 120 amino acids joined together

[2] Bioscience Reports (2018) 38 BSR20181176 https://doi.org/10.1042/BSR20181176
[3] Aging (Albany NY). 2016 Jun;8(6):1259-75. doi: 10.18632/aging.100982.
[4] Case Rep Orthop. 2018; 2018: 5796730. doi: [10.1155/2018/5796730]

Recombinant protein drugs are regulated as biologics and by 2020 the market size for all recombinant protein drugs is projected to be US$600 billion [5] – so while KT009 is novel it is not in an unusual class of drugs.

Other recombinant protein products on the market [6] include :-

Trade Name	**United States Adopted Name/biological description**	**Indication/Sales (2016)**
Epogen	erythropoietin	anemia / US$5 billion
Enbrel	etanercept	rheumatoid arthritis etc. / US$8 billion
Lantus	insulin glargine	glycemic control / US$6 billion

Why did Medigard select this project ?

The story around KT009 is appealing from a number of perspectives, including :

- granted US patents for the main use of KT009
- compelling animal data supporting treatment with KT009, with extensive peer-reviewed publications
- the fact that a deficit of functional KT009 leads to joint malformation in children
- the active agent of KT009 is an endogenous protein i.e. not foreign to the body
- the unmet medical need is large and growing
- a larger company would be expected to partner once Medigard has de-risked the KT009 manufacture and safety/efficacy
- relatively short development program to get to proof of concept in humans
- ability to non-invasively image discs to determine medical outcomes quickly

In short, Medigard saw the KT009 product as a simple yet powerful story. With KT009 there is the potential to both help millions of patients and create financial upside for shareholders.

How will shareholders benefit from investment in KT009 ?

The KT009 development program has been designed to de-risk the KT009 product – in preparation of partnering with a larger orthopaedic or Pharmaceutical company. Typically, such a partnership could deliver to a company like Medigard a combination of cash payments of upfront fees, milestone fees and then royalties on sales. These amounts can be substantial. For example, in November 2018 surgical implant company RTI Surgical entered into a definitive agreement to buy the spinal implant technology company Paradigm Spine in a cash and stock deal worth up to US$300m [7].

Medigard could decide to take KT009 into larger Phase II studies, in a strategy to increase the financial returns to shareholders.

[5] www.creativebiomart.net/blog/market-and-rd-analysis-of-recombinant-protein-drugs/
[6] www.genengnews.com/lists/the-top-15-best-selling-drugs-of-2016/
[7] www.businesswire.com/news/home/20181101006167/en/RTI-Surgical®-Acquire-Paradigm-Spine

What are the next steps to watch out for in the development program ?

The key steps in the KT009 development program are (i) manufacture (ii) preclinical testing and then (iii) small scale clinical study in patients with DDD.

We will keep shareholders up to date with progress over the following months.

Please feel free to contact me any time at ian.dixon@medigard.com.au.

Yours sincerely Ian Dixon

Executive Director

14th November 2018