

## Scarred for life: An Australian case study

**Breathless moments:** a phrase we associate with witnessing indescribable sunsets, experiencing a cultural phenomenon, and being in love. But this isn't the case for everyone. For those suffering from fibrotic conditions, breathless moments are literally a torment.

There are different types of fibrotic conditions – including the well-known cystic fibrosis (CF) that effects one in every 2,500 babies in Australia (one CF child is born every four days) – and the rarer and lesser-known idiopathic pulmonary fibrosis (IPF), a condition that around 1,500 Australians are diagnosed with each year.

### What is fibrosis?

Fibrosis is a medical condition where the body's connective tissue on and between organs succumbs to excessive thickening, hardening and scarring. It forms the same way scars are made on your skin, it's rough, tough and tight – only it's on the inside of your body.

Whilst typically this internal scarring is caused by an injury to the organ's tissue, and/or sometimes through chronic inflammatory reactions from autoimmune responses to some medications, IPF is different. Regrettably, IPF is a disease whose origin is currently unknown. The effects patients suffer from the diseases are irreversible. It affects their body, their wellbeing, and ultimately their lifespan.

### Australian biotechs making a difference

Australia is a global leader within the biotechnology sector, developing world-changing therapeutics with global impact. Two Australian listed companies in this field are working towards re-designing the landscape of fibrosis treatment: AdAlta and Pharmaxis. Each company is developing products that are expected to affect the growth rate of internal fibrotic scarring by slowing and inhibiting it at a cellular level, thereby alleviating some of the difficulty patients have breathing, and subsequently improving their life expectancy.



## **Idiopathic Pulmonary Fibrosis (IPF)**

IPF occurs spontaneously, without a known cause. It is a rare type of lung disease, where the tissue around the air sacs within the lungs become thick and scarred. This scarring hardens the lungs, making it excruciatingly challenging for sufferers to breathe deeply, and for oxygen to be efficiently delivered into the bloodstream. Patients often describe their breathing as sounding like Velcro being torn apart.

### **Fibrosis globally**

In the United States alone, it is estimated that 135,000 people are diagnosed sufferers of IPF. While new diagnoses are made each year, roughly the same number of patients will die from the disease. The global number of IPF sufferers is estimated to be around 800,000 including Europe, USA and China.

IPF is a fatal disease, without any cure. Those with IPF can typically expect total lung deterioration within three-to-five years; 50% of sufferers die within two-to-three years following diagnosis, and only one-fifth of patients survive five years from diagnosis.

**AdAlta (ASX: 1AD)** is a highly innovative drug discovery and development company based in Melbourne. Using proprietary 'i-body technology', its lead drug "AD-214" works by targeting cells in the lung that express a protein called CXCR4, which has been shown to be linked to the disease and significantly upregulated in disease. AD-214 has been designed with two i-body molecules at the front that enhance drug binding to CXCR4 and an Fc fragment at the back that increases the time the drug stays in the body. As a biological drug, AD-214 will be administered via IV infusion, with the longer half-life of AD-214 reducing the frequency of dosing. Patients and their physicians identified reducing the frequency of dosing as important when treating fibrotic diseases. AdAlta is an early-stage company and expects to enter Phase I of clinical trials for its i-body technology in January 2020.

**Pharmaxis (ASX: PXS)** is working on a drug that will decelerate the process of scarring at a cellular level through the suppression of the Lysyl Oxidase Like-2 and 3 enzymes (LOXL2 and LOXL3). These enzymes cause the collagen and elastin fibres that are made by the body in response to tissue damage, and form fibrotic or scar tissue. Other members of this family of enzymes are responsible for healthy scarring and would promote healing; elevated levels of LOXL2 and 3 are only seen in patients with diseases like liver or lung fibrosis, and the higher the levels of these enzymes the poorer the outcomes for patients with these diseases. Pharmaxis' compound inhibits these enzymes and in phase I clinical trials in the latter half of 2018 demonstrated significant and long lasting inhibition from a single daily dose making this a best in class drug. Fibrotic tissue is renewing itself all the time so if you can stop new fibrosis by blocking the crosslinking of tissue fibres then the area of fibrosis should recede and the symptoms and life expectancy of patients with fibrotic disease should be extended. The company has now completed longer term toxicity studies and the company is looking at further developing the drug as a once-a-day oral pill through collaborations with multinational Pharma companies later this year (2019).

## The future

The work these Australian companies are undertaking, once proven in clinical trials, will impact on the lives of both IPF sufferers, locally and globally. Their intentions to alleviate the unforgiving symptoms caused by this condition – in combination with their innovative products – inspires a realistic foundation for hope for patients. The hope is that we will all be able to breathe a little easier.

### About AdAlta Limited

**Based:** Victoria, Australia

**Listed company:** ASX: 1AD

**Chief Executive Officer:** Sam Cobb

**Interested in:** Investment, partnership

**[adalta.com.au](http://adalta.com.au)**

### About Pharmaxis

**Based:** New South Wales, Australia

**Listed company:** ASX: PXS

**Chief Executive Officer:** Gary Phillips

**Interested in:** Partnership

**[pharmaxis.com.au](http://pharmaxis.com.au)**

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