

Pharmaxis Ltd: Case study

Pharmaxis Ltd is an Australian pharmaceutical research company established in 1998. It listed on the Australian Securities Exchange (ASX) in 2003. The business focuses on new therapies to treat inflammation and fibrosis with a portfolio of products at various stages of development and approval. With origins in clinical research, this Australian-owned start up successfully competes in an international market.



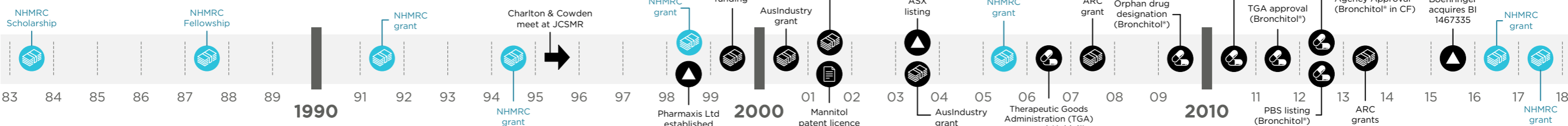
Origin

The Pharmaxis story began in the 1990s when Drs Brett Charlton and William Cowden met at the John Curtin School of Medical Research (JCSMR) at the Australian National University (ANU). They co-founded Pharmaxis (originally named Praxis Inc.) in 1998 to commercialise a group of compounds (patented by ANU) with the potential to treat inflammatory and other immune-mediated diseases.

This initial intellectual property (IP) licence attracted venture capital funding and enabled Pharmaxis to license further patents from ANU and CSIRO. These early licences did not progress to commercial development. However, they created a momentum of activity and interest which, in 2001, allowed Pharmaxis to license IP from the (then) Central Sydney Area Health Service (CSAHS) on the potential of the dry sugar mannitol to diagnose asthma and reduce the symptoms of cystic fibrosis (CF). This patent was developed into Pharmaxis' first products, Aridol® and Bronchitol®, in collaboration with Dr Sandra Anderson AM (University of Sydney) and her colleagues. [See separate NHMRC case study.]



Dry mannitol powder has a number of uses. In Aridol® it is used in aerosol form as a test to identify asthma and assess its severity. In Bronchitol® it assists people with cystic fibrosis to clear their airways of mucus.



Grants and Investment

NHMRC

NHMRC supported Drs Charlton and Cowden early in their careers. Pharmaxis also received Development Grants in association with other institutions.

Brett Charlton:

- Postgraduate Scholarship 1983-84
- Postdoctoral Fellowship, Walter and Eliza Hall Institute (WEHI), 1987-88
- International Collaborations for Diabetes Research Grant, 1998.

William Cowden:

- Targeted Calls for Research Grant, 1991
- Project Grant, 1994.

Pharmaxis, with Professors:

Hak-Kim Chan, University of Sydney, bronchoprovocation testing in children, 2005
Fiona Wood, University of Western Australia, treatment of scars resulting from burns, 2016
Paul Young, Woolcock Institute, testing inhaled antibiotics with the Orbital inhaler, 2017.

Other grants and investment

- Rothschild Bioscience (now GBS Ventures), 1999 and 2001
- AusIndustry START grants, 2000 and 2003
- AusIndustry Biotechnology Innovation Fund grant, 2001
- ASX Initial public offering (IPO), 2003. Approx. \$300 million in capital has been raised from the public markets since the IPO
- Australian Research Council (ARC) Linkage Projects grants: University of Sydney, 2007; Kolling Institute, 2013; and Woolcock Institute, 2013.

Commercialisation Journey

The road to developing a fully viable company took many twists and turns. There were few venture capitalists (VCs) when Charlton and Cowden first established Pharmaxis. Their early suite of patent licences led them to Melbourne-based VC fund GBS Ventures in 1999. GBS commissioned Dr Alan Robertson, then a consultant, to report to them on the company. Based on his report, they committed the first seed funding. Charlton and Cowden hired Robertson as CEO to provide the company with much-needed business experience, and he helped kick-start the company's rapid progression. Clinical trials progressed within 10 years, requiring several rounds of successful capital fund raising. Pharmaxis established its manufacturing facility in Sydney during this period.

Since bringing Aridol® and Bronchitol® to market, the company strengthened its drug discovery capability by hiring experienced international pharmaceutical executives. The company now focuses on developing drugs to Phase I or Phase II clinical trials, and then licensing these drugs to larger pharmaceutical companies. For example, in 2015, Pharmaxis licensed a drug to German-based Boehringer Ingelheim (BI), which BI is now trialling. Pharmaxis receives staged payments based on the success of the trials; to date, these have totalled \$83 million.

Research and Trials

Early research leads were not successful for Pharmaxis but the subsequent licensing of the mannitol patent from CSAHS ultimately led to the clinical trialing and commercial development of Aridol® and Bronchitol®.

Following the recruitment of Ian McDonald in 2005, Pharmaxis built a drug discovery program based on amine oxidase chemistry and now focuses on discovering drugs to treat inflammatory and fibrotic diseases such as the liver disease Non-Alcoholic Steatohepatitis (NASH), pulmonary fibrosis, kidney and liver fibrosis and cancer.

- In 2015, BI acquired the investigational drug BI 1467335 to treat both NASH and Diabetic Retinopathy (DR), a leading cause of blindness. A Phase II clinical trial for NASH commenced in August 2017. A Phase IIa trial for DR commenced in January 2018.
- In 2016, Pharmaxis announced a research collaboration with the Woolcock Institute to develop a therapy for the treatment of CF using the Pharmaxis developed Orbital inhaler technology. Planning for Phase II trials is underway.
- In November 2018, Pharmaxis completed Phase I trials on a molecule that targets the LOXL2 enzyme, which is present in several fibrotic diseases such as NASH. This is the second program from its amine oxidase platform to reach clinical trials.

Outcomes and Impact



Since its foundation in 1998, Pharmaxis has achieved significant milestones for an Australian-owned company. It has:

- developed and manufactured two successful pharmaceutical products (Aridol® and Bronchitol®) to a world-wide market
- developed and maintained ownership of IP in Australia
- developed an internationally-recognised medical research program bringing new drugs to Phase I, II and III trial stages
- established partnerships with other significant research bodies and pharmaceutical companies
- fostered a new generation of medical researchers. Pharmaxis has employed over 100 postgraduate researchers in the fields of drug discovery and development, clinical trial design and management, pharmaceutical manufacturing, business development and capital markets.

Dr Brett Charlton

Dr Charlton is co-founder and Medical Director of Pharmaxis Ltd. He helped to attract funding from a range of public and private investors to develop Aridol® and Bronchitol®. Dr Charlton has been an NHMRC Postdoctoral Fellow at the WEHI and visiting clinician at Royal Melbourne Hospital working on diabetes and autoimmunity. He was a Founding Medical Director of the National Health Sciences Centre in Canberra. In 1995 he was awarded the Aza/Lilly Fellowship from Diabetes Australia.

Dr William Cowden

Dr Cowden is co-founder, and was Chief Scientific Officer (until 2008), of Pharmaxis Ltd. He has spent over 20 years developing new therapeutic compounds for the treatments of cancer, infectious disease, and inflammatory diseases. Dr Cowden has held senior research positions at the JCSMR, Peptide Technology Ltd (Peptech), and consulting scientist to Anutech. He received a PhD in Medical Chemistry from the University of Queensland in 1979. He is the co-inventor on 12 patents and author of over 130 scientific papers.

Dr Alan Robertson

Dr Robertson served as CEO of Pharmaxis Ltd from 1999 - 2013. Prior to this, he held senior product development roles at Wellcome PLC, Faulding Group and Amrad Pty Ltd. Dr Robertson has assisted in the establishment of two start-up companies, Promics Pty Ltd and Pharmaxis Ltd. He is the co-inventor of 18 patents and author of more than 35 scientific papers. He is also the inventor of the migraine therapeutic Zomig. Dr Robertson holds a BSc and a PhD in Synthetic Organic Chemistry from the University of Glasgow.

Gary Phillips

Mr Phillips joined Pharmaxis Ltd in 2003, and was appointed CEO and a director in 2013. He previously held the positions of Commercial Director and Chief Operating Officer. Mr Phillips has more than 30 years of management experience in the pharmaceutical and healthcare industry in Europe, Asia and Australia, including at Ciba Geigy (Hungary), and Novartis Australia. He holds a B Pharm from Nottingham University, UK, and an MBA from Henley Management College. Mr Phillips is a Graduate Member of the Australian Institute of Company Directors.

Dr Ian McDonald

Dr McDonald was the Chief Technical Officer at Pharmaxis Ltd from 2005 - 2012. He has over 25 years of international experience in managing drug discovery and design teams in Europe and USA, including at Structural Genomix, Structural Bioinformatics, SIBIA Neurosciences and Merrell Dow. Under his leadership at Pharmaxis Ltd, six compounds have been developed and evaluated in clinical trials. Dr McDonald was awarded his PhD in Organic Chemistry from the University of WA and has co-authored over 75 peer-reviewed manuscripts and book chapters, and is an inventor on 39 issued US patents.

Dr Wolfgang Jarolimek

Dr Jarolimek joined Pharmaxis Ltd in 2010 as Manager, In Vitro Pharmacology, and was appointed Head of Drug Discovery in 2012. He has more than 20 years' experience in pharmaceutical drug discovery and has published more than 20 peer-reviewed articles. Prior to joining Pharmaxis Ltd, Dr Jarolimek worked at GlaxoSmithKline, Italy, and Merck, Sharp and Dohme, England. He holds a PhD in Pharmacy from the University of Saarbrücken, Germany. In 1997, he became Assistant Professor in Physiology at the University of Heidelberg, Germany.