Pharmaxis Ltd
Risk Management Statement

1. Board responsibility

The Pharmaxis Board is responsible for ensuring the Company establishes and maintains a risk management framework for the oversight and management of risk consistent with the risk appetite set by the Board.

The Board reviews risks to the Company's business plan at its scheduled meetings.

The Audit Committee, at least annually:

- reviews and updates the risk profile of the Company
- reviews the Company's policies and procedures for identifying and managing risk
- makes recommendations to the Board concerning the Company's risk management framework

2. Risk Appetite

The Company has a different approach to risk appetite in relation to the two distinct segments of its operations.

The Bronchitol and Aridol segment manufactures and sells its two approved pharmaceutical products into global markets, predominantly by way of distributors. The pharmaceutical industry is heavily regulated by government so as to ensure the safety of patients. The Company must therefore have a low risk appetite in relation to the operations of this business segment and consequently has developed extensive industry standard systems and approaches to monitor compliance with regulatory requirements in relation to the quality of the pharmaceutical products it manufactures and sells and the monitoring of patients who use the Company's products. The Company also has a low risk appetite in relation to its commercial investment in this business segment. As such it seeks to use specialist distributors to sell its product (outside of Australia) rather than invest in the commercial and logistical infrastructure to directly sell the products to patients and clinicians.

The Pharmaxis New Drug Development segment seeks high returns from its high risk biotech business model. While the Board adopts a higher risk appetite in relation to this segment of the Company, the higher risk appetite is not applicable to all activities of the segment. The higher risk appetite particularly applies to the selection of the therapeutic targets which are the focus of the research programs, rather than to the manner in which the research programs are conducted. The Company conducts extensive reviews before embarking on a research program, seeking input its Scientific Advisory Board and other external key opinion leaders. The Company's research programs are informed by an understanding of the data packages required by big pharma companies who are the likely eventual partners of successful research programs – gained from experience of the Company's key researchers working within big

pharma and by regular engagement with big pharma scientific and business development representatives.

3. Senior executive responsibility

The Chief Executive Officer and the Chief Financial Officer are responsible for profiling the Company's risks and ensuring appropriate risk management procedures are in place and operating effectively consistent with the risk appetite set by the Board. Within this framework, areas of risk are monitored as a part of the regular reporting to the Board.

4. Risk profile and management

The Pharmaxis business has undergone fundamental changes since 2013 that have changed both the opportunities open to the business and the associated risks. An important requirement of the current business plan has been to position the Company such that ongoing operations are predominantly funded by revenues derived from its existing assets. While the capital markets are open to the Company, the business plan is designed to access these only for strategic initiatives to accelerate growth and development.

4.1 Funding risk

As noted above the Company's current business plan is to fund ongoing operations predominantly using revenues derived from its existing business segments. Funding risks associated with the business plan of the Company's two segments include:

New drug development

The largest opportunities pursued by the Company arise from its new drug development segment, which has developed a drug which was sold to Boehringer Ingelheim in 2015 and provides significant ongoing funding to the business. Other drugs are advancing through the new drug development pipeline which the Company plans to partner in coming years. Pharmaxis will aim to partner new drugs at the phase 1 or phase 2 stage of development, but does not plan to undertake extensive and expensive phase 3 clinical trials or regulatory approval and reimbursement processes. These stages of development and commercialisation will be the responsibility of partners. The expenses associated with new drug development are small in the early stages compared to the clinical development phase and the costs only increase as the results of research work justify advancing the specific project towards the clinic. The process to partner is complex, expensive and not quickly achieved. Revenue from partnering new drugs typically takes the form of large payments at irregular intervals, the payment of which is triggered by development milestones over which the Company has no direct control. Pharmaxis seeks to manage the uncertainty of these risks by:

- Focusing its new drug development on biological targets that are of interest and value to potential big pharma partners
- Initiating early engagement with potential partners to inform the drug development process and build scientific credibility

- Leverage the Company's proven research expertise in drug and clinical development to deliver multiple new drug candidates to enter phase 1 & 2 clinical trials
- Selection of partners that are committed to a rapid development of the drug acquired from the Company
- Review of drug development projects by the Company's Scientific Advisory Board
- See also 4.2 Research Risk below

Bronchitol & Aridol

The Bronchitol and Aridol business manufactures and sells, predominantly through distributors, the approved products of the Company. With the completion of a third large international clinical trial in cystic fibrosis in 2017, the large clinical expenditures and risks are now completed. Furthermore, the majority costs associated with selling Bronchitol outside of Australia are the responsibility of the specialist distributors appointed by Pharmaxis. Aridol continues to be sold to international markets with minimal sales and marketing investment by Pharmaxis. The Company believes this segment will transition to profitability as sales in non-US markets grow over the coming years, with Russia being key to the expected sales growth. While additional product and pricing approvals for Bronchitol are expected to lead to further sales growth for Bronchitol, the timing and the outcome of these negotiations are uncertain as is the rate of sales growth once pricing is negotiated.

The US market for Bronchitol is potentially large. The Company's US partner Chiesi filed an updated new drug application with the US FDA in late 2018. Following a positive recommendation from a Pulmonary-Allergy Drugs Advisory Committee meeting convened by the FDA in May 2019, Chiesi received a complete response letter from the FDA in June 2019 detailing the remaining matters to be addressed before Bronchitol can be approved for adult cystic fibrosis patients in the United States. The main requirement included in the FDA complete response letter is that Chiesi revise the product packaging and user instructions; and then conduct a human factor study demonstrating that the revised user components enable healthcare professionals to properly administer the mannitol tolerance test. These remaining requirements are targeted for completion by the end of 2019. Pharmaxis believes that the FDA review of the Bronchitol NDA will be completed in Q1 2020. Subject to the FDA's approval, Chiesi will market Bronchitol in the US. Under its agreement with Chiesi, the Company is entitled to receive US$10 million on the commercial launch of Bronchitol in the US, high mid teen percentage of in-market sales in addition to supply of Bronchitol on a contract manufacturing basis. Subsequent to the delivery of the final study report for study CF303 in late 2017, Pharmaxis has no further investment in relation to the US market until it manufactures Bronchitol for the commercial launch.

Pharmaxis major cost in relation to this business segment is its manufacturing facility which has the fixed cost capacity to support significantly larger sales volumes for minimal additional cost. In addition to the larger opportunities of the Russian and US Bronchitol markets, the Company is

seeking approval and reimbursement of Bronchitol and Aridol through distributors in a number of smaller countries where the increased sales only result in an incremental cost to manufacture. See also 4.4, 4.5 and 4.6 for more detail on the risks associated with this business segment.

R&D tax credit

The Company was entitled to an Australian research and development tax credit of $6.0 million in the 2019 financial year and nil in 2018. The Company expects to be eligible for the tax credit in future years depending upon its ability to meet eligibility criteria, in particular the limit on total revenue of $20 million cap, which was exceeded in the 2018 financial year.

4.2 Research risk:

Risk is inherent in the research and development process. Nevertheless, that risk requires management to ensure adequate justification exists before proceeding to the next phase of development. Pharmaxis manages the risks associated with its research and development activities by:

- Pharmaxis staff having the experience and capability to design and manage its drug development programs to deliver drugs and supporting data packages acceptable to large pharma companies.
- Interacting with large pharma companies as projects proceed to understand their objectives and requirements for new drugs they are looking to acquire.
- Fully documenting all research project plans and monitoring performance against plan on a regular basis.
- Phasing expenditures on individual projects such that continued expenditure is dependent on achievement of milestones.
- Regular reports to and review by Senior Management and Board of Directors.
- Periodic evaluation of proposed research projects against expected business returns.
- Review of research projects by the Company's Scientific Advisory Board and independent consultants.

4.3 Clinical & preclinical risk

Approval of a therapeutic product by a regulatory agency requires the submission of an extensive clinical, preclinical (safety) and manufacturing dossier. The dossier includes the results of the supporting clinical trials and preclinical studies. While the Company's business plan is to partner drug discoveries at either phase 1 or phase 2, the design and completion of these trials must support future phase 3 trials to be completed by partners. In designing clinical trials and preclinical studies it is therefore important to ensure that the endpoints of the trials/studies will be acceptable to potential partners as well as the regulatory agencies in all of the countries where registration will be sought; that the trials/studies will support the desired label claim of the product, and that the trial/study end points to be completed by Pharmaxis are achievable in an acceptable timeframe and at an acceptable cost.

Successful execution of clinical trials and preclinical studies requires negotiation of contracts with acceptable timetables, costs and risks with the various investigators, institutions and clinical research service providers necessary to conduct a clinical program; and constant monitoring of contract performance over the course of the trial/study.

The conduct of preclinical studies involves animal testing at third party research organisations and potentially exposes the Company to adverse publicity or interruption to research activities as a result of activities by animal rights organisations.

The clinical/preclinical program risk is managed by:

- Pharmaxis staff having the experience and capability to design and manage its clinical and preclinical program.
- Regular internal cross functional meetings review both trial/study design and ongoing performance.
- Finalising clinical and preclinical study designs in collaboration with contract research organisations, investigators, regulators and experienced consultants.
- Engaging clinical research organisations with relevant disease experience and global capability to run clinical trials.
- Negotiating contractual arrangements such that payments are, wherever possible, tied to contractual performance.
- Minimising preclinical studies involving animal testing and only conducting such studies at organisations and facilities that meet both industry and Pharmaxis standards of animal welfare.

4.4 Sales and marketing risk:

Pharmaxis' product Aridol is sold in Australia, Europe, South Korea and in late 2018 Aridol was relaunched in the United States. Sales over recent years have been approximately $2 million per annum with minimal investment by the Company in sales and marketing. Sales in 2019 were $ 3.1 million reflecting the US re-launch. The South Korean, Spanish and US markets are served by specialist distributors. Pharmaxis received approval to enter the Canadian market in June 2019 and will launch Aridol there by way of its specialist US distributor.

Pharmaxis' product Bronchitol is currently sold by distributors with experience in the cystic fibrosis market and/or orphan diseases in Germany, the United Kingdom, Italy, Spain, Russia, Turkey, Greece, Switzerland, Denmark, Sweden and the Czech Republic. Bronchitol is sold directly by Pharmaxis in Australia and by specialist logistics agents in Austria without any dedicated individual country sales investment.

Pharmaxis manages the sales & marketing risk by:

- Having an appropriately experienced management team.
- Conducting extensive diligence and review of commercial partners before appointment.
- Maintaining a current and open dialogue with commercial partners concerning their sales and promotional activities.
- Having meaningful incentive arrangements for commercial partners.
- Maintaining relationships with specialist clinicians throughout the world.

4.5 Operational risk:

Pharmaxis' operational risk centres on its manufacturing facilities for the production of Bronchitol and Aridol and includes compliance with regulatory operating requirements, the availability of sufficient approved and available operating capacity to meet demand for product and the manufacture and distribution of product to meet global demand. This risk is managed as follows:

- The Frenchs Forest premises include a licensed manufacturing facility and a licensed laboratory to test/monitor/validate the Company's products. Regulatory agencies such as the Australian TGA and the United States Food and Drug Administration conduct regular audits to ensure compliance by Pharmaxis with its licence requirements. Compliance with regulatory agency licence requirements are monitored by the Safety and Quality Committee and reported to the Board of Directors. The Company monitors and responds to changes in global regulatory requirements.
- Continuous forecasting of market demand, required inventory levels and production requirements.
- Reviewing and mitigating circumstances that could limit both short and long term capacity, including reliance on key manufacturing equipment, significant suppliers of product inputs, etc.
- Workplace health and safety matters are reported to the scheduled meetings of management and the Board.

4.6 Regulatory & pricing reimbursement risk in relation to Bronchitol and Aridol:

The pharmaceutical industry is regulated by government agencies in all major markets. Approval by a country's regulatory agency is required before a product may be sold and in many countries separate approval is also required before the sales price is reimbursed. While these agencies generally have published guidelines describing their requirements for approval applications and timetables to process, requests for approval are considered on a case by case basis and may be subject to requests for large amounts of additional supporting data or extended approval times. This risk is managed by:

- Pharmaxis staff have experience in submitting approval requests to the main regulatory and pricing reimbursement agencies.
- Engagement of qualified and experienced specialist consultants with experience in submitting approval requests to the main regulatory and pricing reimbursement agencies

with which we deal (FDA, EMA, TGA and country-specific health technology assessment committees).

- Engaging with regulatory and pricing reimbursement agencies as early as possible to clarify their expectations and requirements in relation to an approval application
- Ensuring partners appointed to commercialise the Company's products have the required regulatory and pricing capability.
- The use of pharmaceutical products must be monitored and regular safety reporting submitted to government agencies. Pharmaxis uses experienced international monitoring and reporting organisations to comply with its safety monitoring and reporting obligations and conducts regular independent audits of the Company's safety reporting systems and policies. Regulatory agencies such as the Australian TGA conduct regular audits to ensure compliance by Pharmaxis with its licence requirements. Compliance with regulatory agency licence requirements are monitored by the Safety and Quality Committee and reported to the Board of Directors.

4.7 Financial risk:

Financial risk includes:

- Safeguarding of Pharmaxis physical assets.
  The Company takes a range of measures to effectively safeguard physical assets. The Company maintains an appropriate level of insurance covering physical loss of assets.
- Safeguarding against fraud.
  An expenditure approval policy delegating spending within budget and up to set limits to various levels of management supported by a robust financial control system is in place. The Board of Directors receive regular reporting of financial performance against an approved budget. Cash investments are managed within Board approved procedures and policies.
- Credit risk
  The credit risk on both the invested cash funds and the interest on the underlying funds is managed in accordance with a Board of Director approved policy that limits the approved investment instruments to bank deposits and bank accepted commercial bills, limits the term of the investment period, specifies the acceptable counterparty banks and requires monthly reporting of investment details to the Board of Directors. The credit risk on accounts receivable is managed by assessment of financial condition before supplying to major customers and regularly monitoring of outstanding receivables from customers.
- Foreign exchange risk.
  The Company contracts with a number of international organisations and institutions to provide a range of services. In most cases these organisations require payment in their local currency. Pharmaxis does not generally hedge the long term purchasing power of its Australian dollar funds which it uses to pay for this clinical research. However, the Company does limit its exposure to amounts due under contracts by paying non

Australian dollar liabilities as soon as possible after receipt of an invoice and by retaining foreign currency receipts to meet expected short term payment obligations. The Company effectively hedged the majority of its currency risk in relation to the Phase 3 clinical trial in cystic fibrosis as both the payments to the clinical research organisation and the reimbursement from Chiesi were denominated in US dollars.

The Company invoices large foreign currency amounts in relation to assets it has partnered to international pharmaceutical companies and also in relation to the supply of product to certain international markets. Such invoices are monitored and where the size is significant and the settlement date can be reliably predicted the Company utilises foreign exchange forward rate agreements to hedge the receivables. The Company's policy will continue to be reviewed as these cash flows increase.

- Financial and IT risks

  The Company has a financial and management system that provides comprehensive management and oversight of the Company's financial and IT risks. This system is reviewed and tested annually.

4.8 Human resources risk:

The success of Pharmaxis depends on its ability to recruit and retain employees with relevant expertise and experience throughout all levels of the Company. High calibre employees are attracted to Pharmaxis by a number of factors including working environment, career opportunities, personal contribution to growth, responsibility and remuneration.

Pharmaxis has a formal annual employee performance appraisal policy which is linked where appropriate to the payment of performance related bonuses and equity plans.

4.9 Intellectual property risk:

Pharmaxis must appropriately protect and safeguard the intellectual property that underpins the future growth and success of the Company. The Company therefore:

- Maintains appropriate records of its research and development activities.
- Patents innovations it considers have possible commercial value.
- Engages appropriately qualified and experienced patent attorneys.
- Requires all employment agreements to contain confidentiality and intellectual property ownership provisions or to sign confidentiality and intellectual property ownership agreements, as a condition of employment.
- Establishes confidentiality agreements with outside parties before discussing any matters of a confidential nature.
- Monitors developments in competing technologies that seek to address the same or similar clinical end points through different means.

4.10 Public liability risk:

Pharmaxis is exposed to certain risks associated with the conduct of its clinical trials. This risk is managed by:

- Employing appropriately qualified and experienced staff. Clinical operations are led by a Medical Director with extensive experience in designing and running international clinical trials.
- Engaging suitably qualified and experienced contract research organisations to manage clinical trials overall or for defined components of the trial.
- Designing its clinical trials to comply with Good Clinical Practice, which incorporates review and approval of clinical trial protocols by independent investigators as well as ethics committees of each site where clinical trials are conducted.
- Clinical trials are monitored whilst in progress by a safety review board.
- Agreement of clinical trial protocols by relevant regulatory agencies.
- Obtaining an appropriate level of clinical trial insurance from a reputable underwriter.
- Seeking expert advice on clinical trial designs.

The Company is also exposed to certain risks associated with the manufacture and sale of its products for both clinical trials and for commercial sale. This risk is managed by:

- Employing appropriately qualified and experienced management and staff.
- Quality management systems that encompass the entire production process and meet the regulatory agency requirements for a licence to manufacture under Good Manufacturing Practices. The Company's manufacturing plant is audited by the regulatory agencies as part of its licence conditions.
- Obtaining an appropriate level of product and public liability insurance from a reputable underwriter.
- Engaging external consultants to provide expert industry advice on systems and controls processes.

4.11 Other:

- Economic, environmental and social sustainability risks.

  At its current size, scope of operations and stage of development the Company does not have any material exposure to any economic, environmental and social sustainability risks.
- Continuous Disclosure.

  As a listed public company Pharmaxis has externally imposed disclosure requirements by the ASX and its own internal standards of shareholder communications. The Continuous Disclosure and Shareholder Reporting Policy sets out the Company's approach to management in this area. The policy is reviewed and amended each year.

- Insider Trading.

  The Share Trading Policy sets out the Company's approach to management in this area, including appropriate trading black-out periods. The policy is reviewed and amended as necessary each year.
- Cyber security risk.

  Pharmaxis is exposed to cyber security risk in relation to its IT infrastructure which is a mix of internal resources and externally hosted applications. The Company reviews the security measures employed by external service providers and utilises a range of measures to protect its internal IT resources, including specific security hardware and software, physical security surrounding IT infrastructure and staff training.

5. Effectiveness of risk management

This Pharmaxis risk management statement is annually updated by management and reviewed by the Audit Committee in conjunction with a review of the Pharmaxis risk profile. The CEO and CFO must annually attest to the effective operation of the Company's system of risk management.