

1998	0.6208	0.6805	0.7550	0.5867
1999	0.6650	0.6246	0.6745	0.6123
2000	0.5971	0.6237	0.6560	0.5708
2001	0.5100	0.5320	0.5996	0.4828
2002	0.5614	0.5682	0.5747	0.4858

## B. CAPITALIZATION AND INDEBTEDNESS

Not applicable.

## C. REASONS FOR THE OFFER AND USE OF PROCEEDS

Not applicable.

## D. RISK FACTORS

*Investing in our American depositary shares involves a high degree of risk and uncertainty. You should carefully consider the risks and uncertainties described below before investing in our depositary shares. Additional risks and uncertainties not presently known to us or that we believe to be immaterial may also adversely affect our business. If any of the following risks actually occurs, our business, prospects, financial condition and results of operations could be harmed. In that case, the daily price of our depositary shares could decline, and you could lose all or part of your investment.*

### Risks Related To Our Business

**We are a development stage company at an early stage in the development of pharmaceutical products and our success is uncertain.**

We are a development stage company at an early stage in the development of our pharmaceutical products that are designed to treat the underlying causes of degeneration of the brain and the eye as the aging process progresses. We have not sufficiently advanced the development of our lead product candidate, PBT-1, to market or generate revenues from its commercial application. PBT-1 is the code name for clioquinol, an antibiotic drug that was previously used to treat other illnesses until its withdrawal in the 1970's. In the 1960's clioquinol (Iodochlorohydroxyquinoline) was used in the treatment of intestinal amebiasis in doses of 250mg three to four times daily for up to 10 days. It was also used for the prevention and treatment of traveler's diarrhea. Overuse of clioquinol, particularly in Japan was associated with the development of subacute myelo-optic neuropathy. Symptoms included numbness in legs, progressing to paralysis in a small number of patients, loss of visual acuity sometimes leading to blindness, sensory disturbances and a characteristic green pigmentation of the tongue, feces and urine. Most patients improved when clioquinol was withdrawn, however some had residual disablement. It was also suggested that the incidence in Japan was caused by concomitant viral infection, dietary or genetic susceptibility. Clioquinol may rarely cause iodism in sensitive patients. Clioquinol for oral use was withdrawn from the market in early 1970's, but it continues to be available in some countries for topical use for treatment of skin infections.

PBT-1 acts as metal chelator that prevents the formation of hydrogen peroxide and therefore free radical formation by removal of excess copper and dissolving plaques by removing the metals from existing plaques. In the early 1990's Professor Ashley Bush, now a member of our Scientific Advisory Board observed the A Beta protein (the primary constituent of plaque) binds to zinc and copper in the brains of Alzheimer's patients that contained three to four times as much zinc, copper and iron as normal, and that the metals were largely concentrated in the plaque. Prana is developing new chemical entities through rational drug design techniques which may result in the formation of new compounds that provide more effective therapies than PBT-1. PBT-1 and any future pharmaceutical product candidates will require significant additional investment in research and development, pre-clinical testing and clinical trials, regulatory and sales and marketing activities, and regulatory approval prior to any commercial sales. We cannot make any assurances that PBT-1 or any other product candidates, if successfully developed, will generate sufficient or sustainable revenues to enable us to be profitable.

**There is a high risk that we may not be able to complete the development of PBT-1 or develop other pharmaceutical products.**

We cannot make any assurances that we will be able to develop PBT-1 or any future pharmaceutical product candidates adequately to attract a suitable collaborative partner, or that our research will lead to the discovery of additional product candidates, or that any of our current and future product candidates will be successfully developed, prove to be safe and efficacious in clinical trials, meet applicable regulatory standards and receive regulatory approval, be capable of being produced in commercial quantities at reasonable costs, or be successfully or profitably marketed,

either by us or a collaborative partner. We also cannot make any assurances that the

products we develop will be able to penetrate the potential market for a particular therapy or indication or gain market acceptance among health care providers, patients and third-party payors. We cannot predict if or when PBT-1 or any of our other pharmaceutical products under development will be commercialized.

**The results of clinical trials of PBT-1 are uncertain and we will not be able to commercialize PBT-1 or any of our other product candidates if we fail to adequately demonstrate their safety, efficacy and superiority over existing therapies.**

Before obtaining regulatory approvals for the commercial sale of any of our pharmaceutical products, we must demonstrate through pre-clinical testing and clinical studies that our product candidates are safe and effective for use in humans for each target indication. Conducting pre-clinical testing and clinical studies is an expensive, protracted and time-consuming process. Likewise, results from early clinical trials may not be predictive of results obtained in large-scale, later-stage clinical testing. In addition, even though a potential drug product shows promising results in clinical trials, regulatory authorities may not grant the necessary approvals without sufficient safety and efficacy data.

We have completed initial phase II human clinical trials of PBT-1 at our sponsored facilities at the Royal Melbourne Hospital and the Mental Health Research Institute, both based in Melbourne. We have utilized the services of Kendle Pty Ltd, or Kendle, the Australian subsidiary of the U.S. based clinical development organization Kendle International, to assist us in coordinating, planning, managing and monitoring these trials and with planning and advice in relation to the structure and commencement of additional clinical trials. Under the terms of our strategic alliance agreement with Kendle, they are paid a daily fee of A\$1,200 for such services. We cannot make any assurances that we will be able to commence additional clinical trials of PBT-1 as planned, or at all, or to demonstrate the safety and efficacy or superiority of PBT-1 over existing therapies, or other therapies under development, or enter into any collaborative arrangement to commercialize PBT-1 on terms acceptable to us, or at all. Clinical trial results that show insufficient safety and efficacy could have a material adverse effect on our business, financial condition and results of operations.

**We may experience delays in our clinical trials that could adversely affect our business and operations.**

We do not know whether planned clinical trials will begin on time or whether we will complete any of our clinical trials on schedule or at all. Our ability to commence and complete clinical trials may be delayed by many factors, including:

- Government or regulatory delays, including delays in obtaining approvals from applicable hospital ethics committees and internal review boards;
- Slower than expected patient recruitment;
- Our inability to manufacture sufficient quantities of PBT-1 or our other product candidates;
- Unforeseen safety issues; and

- Lack of efficacy or unacceptable toxicity during the clinical trials.

Patient enrollment is a function of, among other things, the nature of the clinical trial protocol, the existence of competing protocols, the size and longevity of the target patient population, and the availability of patients who comply with the eligibility criteria for the clinical trial. Delays in planned patient enrollment may result in increased costs, delays or termination of clinical trials. Moreover, we rely on third parties to assist us in managing and monitoring clinical trials. Any failure by these third parties to perform under their agreements with us may cause the trials to be delayed or result in a failure to complete the trials.

Product development costs to our collaborators and us will increase if

we have delays in testing or approvals or if we need to perform more or larger clinical trials than planned. Significant delays could have a material adverse effect on the commercial prospects of our product candidates and our business, financial condition and results of operations.

**We have limited manufacturing experience, and delays in manufacturing sufficient quantities of PBT-1 for pre-clinical and clinical trials may negatively impact our business and operations.**

We cannot make any assurances that we will be able to manufacture sufficient quantities of PBT-1 or any of our other product candidates in a cost-effective or timely manner. Any delays in production would delay our pre-clinical and phase II human clinical trials which could have a material adverse effect on our business, financial condition and results of operations.

We may be required to enter into contracting arrangements with third parties to manufacture PBT-1 and our other product candidates for large-scale, later-stage clinical trials. We cannot make any assurances that we will be able to make the transition to commercial production. We may need to develop additional manufacturing resources, enter into collaborative arrangements with other parties who have established manufacturing capabilities, or have third parties manufacture our products on a contract basis. We cannot make any assurances that we will have access on acceptable terms to the necessary and substantial financing that would be required to scale-up production and develop effective commercial manufacturing processes and technologies. We also cannot make any assurances that we will be able to enter into collaborative or contracting arrangements on acceptable terms with parties that will meet our requirements for quality, quantity and timeliness.

**We will require substantial additional financing in the future to sufficiently fund our operations and research.**

We have been unprofitable to date and expect to incur losses over the next several years as we expand our drug discovery and development programs and pre-clinical testing and as we conduct clinical trials of PBT-1 and our other product candidates. Although our future capital requirements will depend on many factors, we believe that our existing cash and cash equivalents, potential financing and revenue resources will be adequate to satisfy the requirements of our current and planned operations for the foreseeable future. We cannot, however, make any assurances that such funds will be sufficient to meet our actual operating expenses and capital requirements during such period. Our actual cash requirements may vary materially from those now planned and will depend upon numerous factors, including:

- The continued progress of our research and development programs;

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- The timing, scope, results and costs of pre-clinical studies and clinical trials;
  - The cost, timing and outcome of regulatory submissions and approvals;
  - Determinations as to the commercial potential of our product candidates;
  - Our ability to successfully expand our contract manufacturing services;
  - Our ability to establish and maintain collaborative arrangements;
  - The status and timing of competitive developments; and
  - Other factors.

We anticipate that we will require substantial additional funds in order to achieve our long-term goals and complete the research and development of our pharmaceutical product candidates. In addition, we will require additional funds to pursue regulatory clearances, and defend our intellectual property rights, establish commercial scale manufacturing facilities, develop marketing and sales capabilities and fund operating expenses. We have no established bank financing arrangements, and we cannot be certain that we will be able to establish such arrangements on satisfactory terms, or at all. We intend to seek such additional funding through public or private financings and/or through strategic alliances or other arrangements with corporate partners. We cannot, however, be certain that such additional financing will be available from any sources on acceptable terms, or at all, or that we will be able to establish strategic alliances or other arrangements with corporate partners on acceptable terms, or at all. Any shortfall in funding could result in our having to curtail our operations, including our research and development activities, which could have a material adverse effect on our business, financial condition and results of operations.

**We have a history of operating losses and may not achieve or maintain profitability in the future.**

We have incurred losses in every period since we began operations in 1997. We expect to continue to incur additional operating losses over at least the next several years and to increase our cumulative losses substantially as we expand our research and development and pre-clinical activities and commence additional phase II human clinical trials of PBT-1. We reported a net loss of A\$5,448,467, A\$4,138,979 and A\$1,326,288 during the fiscal years ended June 30, 2002, 2001 and 2000, respectively. As of June 30, 2002, our accumulated deficit was A\$10,994,424. We cannot assure you that we will achieve or maintain profitability.

**Our success depends upon our ability to protect our intellectual property and our proprietary technology.**

Our success will depend in large part on whether we can:

- Obtain and maintain patents to protect our own products;
- Obtain licenses to the patented technologies of third parties;

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- Operate without infringing on the proprietary rights of third parties; and
  - Protect our trade secrets and know-how.

Patent matters in biotechnology are highly uncertain and involve complex legal and factual questions. Accordingly, the availability and breadth of claims allowed in biotechnology and pharmaceutical patents cannot be predicted. While we intend to seek patent protection for our therapeutic products and technologies, we cannot be certain that any of the pending or future patent applications filed by us or on our behalf will be approved, or that we will develop additional proprietary products or processes that are patentable or that we will be able to license any other patentable products or processes.

Our commercial success will also depend, in part, on our ability to avoid infringement of patents issued to others. If a court determines that we were infringing any third party patents, we could be required to pay damages, alter our products or processes, obtain licenses or cease certain activities. We cannot be certain that the licenses required under patents held by third parties would be made available on terms acceptable to us or at all. To the extent that we are unable to obtain such licenses, we could be foreclosed from the development, manufacture or commercialization of the product requiring such license or encounter delays in product introductions while we attempt to design around such patents, and any of these circumstances could have a material adverse effect on our business, financial condition and results of operations.

We may have to resort to litigation to enforce any patents issued or licensed to us or to determine the scope and validity of third party proprietary rights. Any such litigation, regardless of outcome, could be expensive and time consuming, and adverse determinations in any such proceedings could prevent us from developing, manufacturing or commercializing our products and could have a material adverse effect on our business, financial condition and results of operations.

**Our products may infringe on the intellectual property rights of others, which could increase our costs and negatively affect our profitability.**

Third parties may assert against us infringement claims or claims that we have infringed a patent, copyright, trademark or other proprietary right belonging to them. Any infringement claim, even if not meritorious, could result in the expenditure of significant financial and managerial resources and could negatively affect our profitability.

We are currently in litigation in the United States District Court for the District of Columbia concerning the inventorship of our lead compound, PBT-1. If we are not successful in this litigation, our future prospects may be materially impacted. In such a situation we may be required to license certain rights from P.N. Gerolymatos S.A., or be required to develop a molecule with similar metal binding characteristics that will act as an inhibitor in the oxidation process. We cannot provide any assurance that we will be able to obtain such a license, if required, or that we will be successful in developing such a molecule.

**If we do not obtain the necessary governmental approvals we will be unable to commercialize our pharmaceutical products.**

Our ongoing research and development activities are, the production and marketing of our pharmaceutical product candidates derived therefrom will be, subject to regulation by numerous governmental authorities in Australia, principally the Therapeutics Goods Administration, or TGA, and by the Food and Drug Administration, or FDA, in the United States, the Medicines Control Agency in the United Kingdom and the European Medicines Evaluation Authority. Prior to marketing, any therapeutic product developed must undergo rigorous pre-clinical testing and clinical trials, as well as an extensive regulatory approval process mandated by the TGA and, to the extent that any of our pharmaceutical products under development are marketed abroad, by foreign regulatory agencies including the FDA in the United States and the Medicines Control Agency in the United Kingdom. These processes can take many years and require the expenditure of substantial resources. Delays in obtaining regulatory approvals would adversely affect the development and commercialization of our pharmaceutical product candidates. Although we intend to make use of fast-track and abbreviated regulatory approval programs when possible, we cannot be certain that we will be able to obtain the clearances and approvals necessary for clinical testing or for manufacturing and marketing our pharmaceutical products candidates.

**Our research and development efforts will be seriously jeopardized if we are unable to retain key personnel and cultivate key academic and scientific collaborations.**

Our future success depends to a large extent on the continued services of our senior management and key personnel, especially Professors Colin Masters and Ashley Bush. We have entered into consulting agreements with both of these individuals and have obtained key man life insurance policies in the amounts of A\$1 million and A\$2 million with respect to Professors Masters and Bush, respectively. The loss of their services or other key personnel, could negatively affect our business. Our success is highly dependent on the continued contributions of Professors Masters and Bush and our other scientific personnel and on our ability to develop and maintain important relationships with leading academic institutions and scientists. Our dependence on their services has been mitigated to some extent because our company is now at the stage of developing therapeutic drugs which are based on the targets identified by these scientists. Competition among biotechnology and pharmaceutical companies for qualified employees is intense, and we cannot be certain that we will be able to continue to attract and retain qualified scientific and management personnel critical to our success. We also have relationships with leading academic and scientific collaborators who conduct research at our request or assist us in formulating our research and development strategies. These academic and scientific collaborators are not our employees and may have commitments to, or consulting or advisory contracts with, other entities that may limit their availability to us. In addition, these collaborators may have arrangements with other companies to assist such companies in developing technologies that may prove competitive to ours.

**If we are unable to successfully keep pace with technological change or with the advances of our competitors, our technology and products may become obsolete or non-competitive.**

The biotechnology and pharmaceutical industries are subject to rapid and significant technological change. Our competitors in Australia and elsewhere are numerous and include

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major pharmaceutical companies, biotechnology firms, universities and other research institutions. These competitors may develop technologies and products that are more effective than any that we are developing, or which would render our technology and products obsolete or non-competitive. Many of these competitors have greater financial and technical resources and manufacturing and marketing capabilities than we do. In addition, many of our competitors have much more experience than we do in pre-clinical testing and human clinical trials of new or improved drugs, as well as in obtaining FDA, TGA and other regulatory approvals.

We know that competitors are developing or manufacturing various technologies or products for the treatment of diseases that we have targeted for product development. Some of these competitive products use therapeutic approaches that compete directly with certain of our product candidates. Our ability to further develop our products may be adversely affected if any of our competitors were to succeed in obtaining regulatory approval for their competitive products sooner than us.

**Acceptance of our products in the marketplace is uncertain, and failure to achieve market acceptance will negatively impact our business and operations.**

We cannot make any assurances that our products will achieve market acceptance even if they are approved by the TGA and the FDA. The degree of

market acceptance of our products will depend on a number of factors, including:

- The receipt and timing of regulatory approvals for the uses that we are studying;
- The establishment and demonstration to the medical community of the safety, clinical efficacy and cost-effectiveness of our product candidates and their potential advantages over existing therapeutics and technologies; and
- The pricing and reimbursement policies of governments and third-party payors.

Physicians, patients, payors or the medical community in general may be unwilling to accept, use or recommend any of our products.

**The failure to establish a sales, marketing and distribution capability would materially impair our ability to successfully market and sell our pharmaceutical products.**

We currently have no experience in marketing, sales or distribution of pharmaceutical products. If we develop any commercially marketable pharmaceutical products and decide to perform our own sales and marketing activities, we will require additional management, will need to hire sales and marketing personnel, and will require additional capital. We cannot make any assurances that qualified personnel will be available in adequate numbers or at a reasonable cost, that additional financing will be available on acceptable terms, or at all, or that our sales staff will achieve success in their marketing efforts. Alternatively, we may be required to enter into marketing arrangements with other parties who have established appropriate marketing, sales and distribution capabilities. We cannot make any assurances that we will be able to enter into marketing arrangements with any marketing partner or that if such arrangements are established, our marketing partners will be able to commercialize our products successfully.

Other companies offering similar or substitute products may have well-established and well-funded marketing and sales operations in place that will allow them to market their products more successfully. Failure to establish sufficient marketing capabilities would materially impair our ability to successfully market and sell our pharmaceutical products.

**If healthcare insurers and other organizations do not pay for our products, or impose limits on reimbursement, our business may suffer.**

The drugs we hope to develop may be rejected by the marketplace due to many factors, including cost. The continuing efforts of governments, insurance companies, health maintenance organizations and other payors of healthcare costs to contain or reduce healthcare costs may affect our future revenues and profitability and those of our potential customers, suppliers and collaborative partners, as well as the availability of capital. In Australia and certain foreign markets, the pricing or profitability of prescription pharmaceuticals is already subject to government control. We expect initiatives for similar government control at both the state and federal level to continue in the United States. The adoption of any such legislative or regulatory proposals could have a material adverse effect on our business and prospects.

Our ability to commercially exploit our products successfully will depend in part on the extent to which reimbursement for the cost of our products and related treatment will be available from government health administration authorities, private health coverage insurers and other organizations. Third-party payors, such as government and private health insurers, are increasingly challenging the price of medical products and services. Uncertainty exists as to the reimbursement status of newly approved health care products thereafter and in foreign markets, including the United States. If third-party coverage is not available to patients for any of the products we develop, alone or with collaborators, the market acceptance of these products may be reduced which may adversely affect our future revenues and profitability. In addition, cost containment legislation and reductions in government insurance programs may result in lower prices for our products and could materially adversely affect our ability to operate profitably.

**We may be exposed to product liability claims, which could harm our business.**

The testing, marketing and sale of human health care products also entails an inherent risk of product liability. We may incur substantial liabilities or be required to limit development or commercialization of our products if we cannot successfully defend ourselves against product liability claims. Although we maintain A\$10 million of no fault compensation insurance with respect to our clinical trial, an amount we believe to be sufficient under the circumstances, we cannot be certain that such coverage will adequately protect us in the event of a successful claim. No assurance can be given that we will be able to obtain product liability insurance in the event of the commercialization of a product or that it will be available

on commercially reasonable terms. Even if we have adequate insurance coverage, product liability claims or recalls could result in negative publicity or force us to devote significant time, attention and financial resources to those matters.

**Changes in government legislation and policy may adversely affect us.**

While we do not anticipate in the near future any specific material changes in government legislation that may adversely affect us, any material changes in interest rate,

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exchange rate, relevant taxation and other legal regimes and government policies may adversely affect us and the market price of our securities.

**We are dependent upon a sole supplier of our key component and could incur significant costs if we are unable to promptly find a replacement.**

Our lead compound, PBT-1 is manufactured by one manufacturer, the Institute of Drug Technology Limited, from whom we have sourced PBT-1 for two years. We have not had any prior manufacturer of PBT-1 cease its relationship with our company. Although we believe that PBT-1 can be obtained from other contract manufacturers since the active ingredient is available as pharmaceutical grade material from other sources, we cannot assure you that we will be able to promptly find a replacement manufacturer without incurring material additional costs.

***Risks Relating to Our Location in Australia***

**It may be difficult to enforce a judgment in the United States against us and most of our officers and directors or to assert U.S. securities laws claims in Australia or serve process on most of our officers and directors.**

We are incorporated in Australia. All of our executive officers and directors are nonresidents of the United States. Therefore, it may be difficult for an investor, or any other person or entity, to enforce a U.S. court judgment based upon the civil liability provisions of the U.S. federal securities laws in an Australian court against us or any of those persons or to effect service of process upon these persons in the United States. Additionally, it may be difficult for an investor, or any other person or entity, to enforce civil liabilities under U.S. federal securities laws in original actions instituted in Australia.

***Risks Relating to Our Ordinary Shares***

**Our stock price may be volatile and the U.S. trading market for our American depositary shares is limited.**

The market price for our securities, like that of the securities of other pharmaceutical and biotechnology companies, has fluctuated substantially and may continue to be highly volatile in the future. The market price for our ordinary shares has ranged from as low as A\$0.32 to a high to A\$2.60 during the last two years. The market price for our ordinary shares has been affected by both broad market developments and announcements relating to actual or potential developments concerning products under development. We believe that the following factors, in addition to other risk factors described above and elsewhere in this annual report, will continue to significantly affect the market price of our ordinary shares:

- The results of pre-clinical testing and clinical trials by us and our competitors;
- Developments concerning research and development, manufacturing, and marketing alliances or collaborations by us and our competitors;
- Announcements of technological innovations or new commercial products by us and our competitors;
- Determinations regarding our patent applications and those of others;

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- Publicity regarding actual or potential results relating to medicinal products under development by us and our competitors;
  - Proposed governmental regulations and developments in Australia, the U.S. and elsewhere;