NDF RESEARCH

Providing independent research coverage of ASX-listed Life Science companies

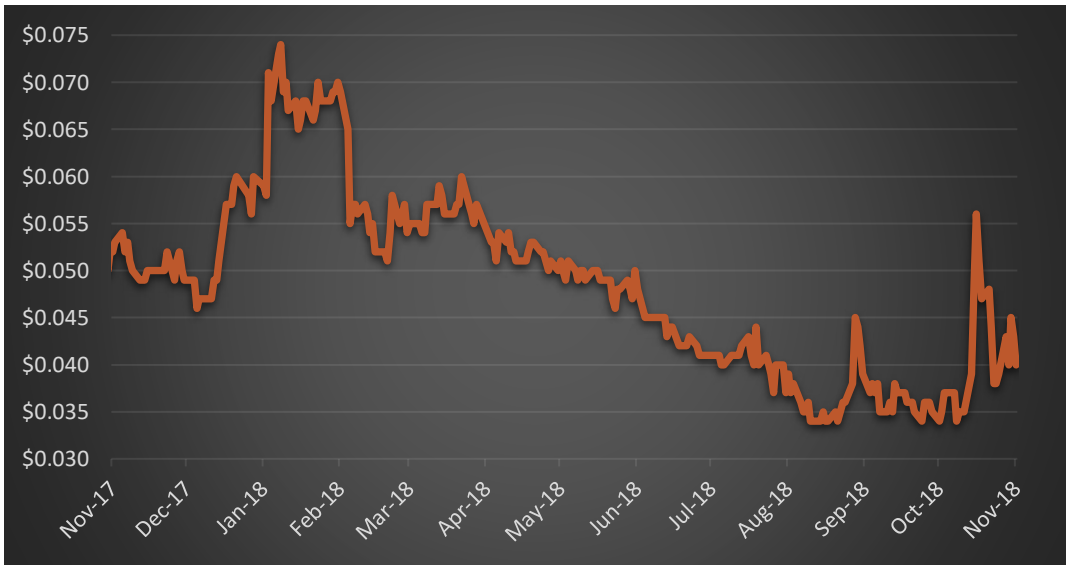
PharmAust (ASX: PAA)

Initiation of Coverage – Monday 5 November 2018

Drug reformulation play with significant potential

PharmAust is a clinical stage company focused on repurposing its lead product MPL, which is already marketed for parasitic infections in sheep. PharmAust also benefits from revenues ($3.0M+) through its wholly owned subsidiary, Epichem that specializes in product sales and services in synthetic and medicinal chemistry. PharmAust's lead drug, being a potential mTOR inhibitor, is being repurposed for the treatment of various forms of cancers in dogs and humans. The company plans to use an integrated approach of simultaneous evaluation of MPL in dog and human cancers to save time and costs. Based on data from early-stage trials, MPL seems to be effective in a range of solid tumors despite being shown to have a high safety profile with minimal toxicities in man and canines. Moreover, the company has already made significant progress with its reformulation to overcome palatability issues, which have been challenging in dosing of both canines and humans. With this progress and the central role of the mTOR pathway, it seems that MPL can open an avenue of new opportunities for PharmAust in not only various forms of cancers but also non-cancer indications. We value PharmAust at 10 cents per share base case and 21 cents per share optimistic case. Our target price of 15 cents sits at the midpoint of our valuation range.

Rating	Risk	Current price	Target price
Buy	High	$0.040	$0.15



Stock details

Daily Turnover: ~A32,000
Market Cap: A8.0m
Shares Issued: 199.0m
52-Week High: $0.074
52-Week Low: $0.034

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About NDF Research

NDF is an independent equity research firm based in Sydney, Australia. It focuses on Life Science companies that are publicly traded on the Australian Securities Exchange (ASX), most of which are headquartered in Australia and New Zealand. ASX hosts one of the world's premier equity markets for biotech and medical device companies and is home to world-beating companies such as CSL and ResMed and emerging pioneers such as Mesoblast and Impedimed.

NDF's Founder and Senior Analyst, Stuart Roberts, has been involved in Life Sciences since 2002 as a sell-side analyst as well as an executive of two ASX-listed immuno-oncology drug developers.

NDF believes that ASX-listed companies have been largely overlooked in the global Life Sciences boom that began in late 2008, partly because of insufficient quality research. NDF's goal is to provide such research and introduce investors around the world to potential future billion-dollar companies from 'Down Under'.

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Ferry at the end of a rainbow on Sydney Harbour, August 2014

In this report

Introducing PharmAust, ASX: PAA

PharmAust is an Australia-based clinical-stage company that develops targeted cancer therapies for human and animal healthcare. Founded in 2000 and operating in various fields for many years, in 2013 Pitney Pharmaceuticals was reversed into PharmAust to create the current structure focused on two wholly owned subsidiaries (Pitney Pty Ltd and Epichem Ltd). The business operates as a drug discovery and development company and focuses on repurposing marketed drugs. Monepantel (MPL), PharmAust's leading drug candidate, is a small molecule marketed for the treatment of parasitic infections in sheep (by Elanco). MPL, one of the most promising products in the company's pipeline, is being investigated in Phase I/II trials. It acts as a modulator of the mTOR pathway that eventually drives the treatment of cancers.

PharmAust operates 2 fully owned subsidiaries – Epichem and Pitney Pharmaceuticals. Established in 2003, Epichem delivers synthetic and medicinal chemistry services to pharma companies across 32 countries and has a highly credentialed team of 23 members, including 15 PhDs. It leads drug discovery programs, performs custom synthesis and optimization, and creates various pharma reference standards to help the industry detect and measure impurities. Epichem also undertakes its own IP-generating research. The 2nd subsidiary, Pitney Pharmaceuticals – acquired by PharmAust in 2013 – develops oncology technology platforms to improve outcomes of patients with inoperable and terminal cancers. With the acquisition of Pitney Pharmaceuticals, PharmAust obtained access to 3 oncology technology platforms – comprising an anthelminthic active drug (MPL), the Albendazole anthelminthic drug[1], and the use of specific enzymes with a mucolytic formulation[2]. The latter two research programmes were subsequent assigned to NewSouth Innovations of the University of New South Wales in exchange for the rights to monepantel (MPL).

MPL IS AN OPPORTUNITY FOR SUSTAINED GROWTH

MPL is a lucrative opportunity for PharmAust. Results from Phase I/II trials that evaluated MPL in solid tumors in human and veterinary cancers are encouraging[3,4]. Other approved drugs operating through the mTOR pathway (mechanistic target for rapamycin) such as everolimus and rapamycin have found commercial success in the field of cancer. These results indicate that MPL may have high potential to address the unmet need for new drugs in the cancer market. Moreover, PharmAust focuses on clinical development of MPL in advanced metastatic and rapidly developing non-metastatic cancers with low survival rates and no effective treatments. This strategy is expected to benefit PharmAust due to short clinical trial time (as low survival time may decrease overall treatment time, leading to faster availability of data), thus reducing the cost of development. Additionally, the fact that the drug has undergone extensive R&D and its registration program is funded by a major pharma company (Novartis Animal Health[5]) for veterinary parasitic infections lowers the risk and costs even further. Meanwhile, the discovery by PharmAust that MPL potentially suppresses cancer activity and shows synergy with chemotherapy in preclinical models has led the company to explore its combination with standards of care. In late 2017, the

[1] See WO/2006/024092 and WO/2006/060853.
[2] See WO/2014/094041.
[3] In a Phase II dog lymphoma trial, 6 out of 7 dogs (86%) contracted a stable disease, 1 dog (14%) developed a progressive disease, and there was a median reduction of 4% in tumor size.
[4] In a Phase I clinical trial, MPL was found to be well-tolerated, leading to reduction in levels of the p70S6K and p-4E-BP1 markers; tumor measurements in 4 patients revealed that 2 patients had a stable disease and 2 patients had a progressive disease.
[5] Novartis Animal Health was acquired by Elanco in 2014.

company also secured a broad patent in the US for MPL's non-cancer applications (including neurodegenerative diseases, diabetes, and age-related disorders). This evidence strongly suggests that MPL not only provides a near-term opportunity but can also support PharmAust's growth in the long term.

Eleven reasons to look at PharmAust

1) **MPL has a higher possibility of success.** Novartis Animal Health (now Elanco) has already conducted extensive studies and has obtained approval for MPL for the treatment and control of gastrointestinal nematode infections in sheep. Considering the fact that PharmAust is piggy-backing on existing programs and data developed by a major pharma player, the risk of development failure is expected to be significantly lower than that associated with new drug development. Prior knowledge may also expedite the approval process.
2) **MPL has unusually low toxicity for an anticancer drug.** The fact that MPL is already approved for the treatment of parasitic diseases in food-chain animals implies that a substantial body of toxicology is available. From the published approval dossiers for MPL in veterinary use (Novartis Animal Health), it is clear that MPL offers a very high safety margin and low toxicity as compared to traditional anti-cancer drugs. In view of the fact that toxicity is one of the main limiting factors in chemotherapy, these safety aspects of MPL bode well for a new generation of anti-cancer drug.
3) **MPL repurposing is expected to shorten development time and lower development costs.** Typically, the drug development process takes 10+ years and involves ~US$1–2 billion in costs. However, as MPL is already approved and is being repurposed for cancer indications, PharmAust is expected to save at least 3–6 years in its clinical development by forgoing the need to conduct discovery and preclinical studies. With lower requirements for preclinical or pilot human safety trials, the cost of taking a repositioned drug through the clinical development and approval processes is anticipated to be significantly lower than the cost of developing a new drug. Moreover, with the dual development strategy, the company intends to translate cancer treatment from pet dogs to humans. The strategy is expected to afford significant benefits to PharmAust considering that it is highly predictive, lowers risk of failure, and provides high-quality preclinical data.
4) **MPL may offer significant advantages over standards of care.** Unlike chemotherapies, that kill cancer as well as normal cells by stopping growth, MPL works by arresting cancer cell replication. Moreover, it is not an immunosuppressant, like chemotherapy or other approved mTOR inhibitors (such as Afinitor and Rapamune), and hence is favorable for the immune system. These properties provide MPL added advantages over the existing drugs for both animal and human use.
5) **New MPL-related compounds (aminoacetonitrile compounds) with 6x greater anticancer activity may provide an opportunity for sustained growth and pipeline.** PharmAust reported that during the initial screening of its proprietary library of aminoacetonitrile (AAD) compounds[6], molecules were identified that

[6] Acquired from Nihon Nohkayu to develop the company's own proprietary pipeline of cancer drugs.

had the potential to kill cells grown in vitro up to 6x more effectively than MPL. The development of MPL analogues will allow PharmAust to commercialize the technology without restriction from any third parties.

6) **Reformulation of MPL bodes well for PharmAust.** PharmAust has reported that micronization of MPL by BRI Pharmaceuticals has successfully met the company's minimum requirements for dosing, taste masking, and oral bioavailability, while in October 2018 the company indicated that absorption and pharmacokinetic studies had gone very well. Considering that PharmAust is able to overcome the recruitment challenges with its new formulation, the drug is expected to be able to make up for the time lost in early-phase trials.
7) **Option agreement with Elanco secures commercial partnership opportunities.** The agreement with Elanco, forged in 2018, provides PharmAust with a secure supply of GMP-grade MPL and will help build a relationship with a potential commercial partner.
8) **A stronger hold on MPL through broader patent protection provides a growth opportunity for PharmAust in non-cancer indications.** In 2017, PharmAust secured a patent in Europe covering its intellectual property for cancer and non-cancer indications with protection until 2033. The activity in non-cancer indications, including neurodegenerative diseases (e.g., Parkinson's disease), diabetes, and age-related disorders, provides an opportunity to use not only MPL but also other aminoacetonitrile derivatives in a broader set of indications.
9) **PharmAust is growing Epichem to tap opportunities in the growing global drug discovery services market.** The increasing inclination of major pharma companies toward outsourcing activities related to clinical trials and increasing R&D expenditure is expected to boost demand for Epichem's services. PharmAust expanded its laboratory space by ~50% in May 2018 in order to accommodate the new business.
10) **PharmAust has a solid and experienced management team.** PharmAust's management team is led by its Chairman and acting CEO, Dr. Roger Aston, who has >20 years' experience in the pharma industry on aspects such as product registration, clinical trials, global licensing agreements, and fundraising. Backing Aston is a well-equipped board that has the capability to build a successful life sciences company, and an advisory committee with renowned names in the veterinary space.
11) **Attractive Valuation.** We believe that with success in the Phase II efficacy trial due to start late in early 2019, a number of substantive commercial opportunities emerge including expansion of the Elanco Option Agreement into a licence and rapid progress of human trials based on success with canine product development. We value PharmAust at 10 cents per share base case and 21 cents per share optimistic case. Our target price of 15 cents sits at the midpoint of our valuation range.

PHARMAUST'S MPL IS BACKED BY DATA FROM LARGE PHARMA COMPANIES AND SUSTAINED SUPPLY FOR CLINICAL TRIALS

PharmAust is repurposing Monepantel

PharmAust's rationale for repurposing MPL is that it provides a capital-efficient path to market. Repurposing MPL is expected to benefit PharmAust in terms of data accumulation and safety. Other companies, including Novartis Animal Health (now Elanco), have already spent millions to collect data on pharmacology, formulation, and safety profile of MPL. This data can provide a head start of at least 3–6 years to MPL's position in various

cancer indications (in both pet and human cancers) and save PharmAust the time and funds required during early-stage trials. Furthermore, MPL is Elanco's product and as such the commercial partner has substantive knowledge and interest in the lead molecule of PharmAust.

PharmAust has a dual clinical development strategy for veterinary and human cancers. The firm's approach is driven by the fact that translation of new cancer treatments from pet dogs to humans offers 3-fold strategic benefits – it is highly predictive, lowers risk of failure, and provides high-quality preclinical data. Many studies validate the use of dog models in studying cancer biology. These studies suggest that there are genetic similarities in oncogenesis between dogs and humans, including specific cancer-associated genes – BRAFV600E, p53, Bcr-Abl, c-kit[7], etc. Moreover, studies indicate that cancers in dogs show the same interplay of genetics, age, and environmental exposures as in humans, and that these similarities are stronger than they are between humans and mice[8]. As cancers in dogs share many features with human cancers, the 'integrated' approach is expected to result in significant cost and time advantages. It is also worth bearing in mind that most canine cancer therapies are modified dosage forms of the corresponding human therapies.

PHARMAUST IS INVESTING IN REFORMULATION OF MPL

The company is investing significant effort in reformulating MPL to improve palatability of MPL and consequently, patient compliance and resolve recruitment challenges. Although a substantial amount of time was lost due to palatability issues during Phase I trials of MPL[9], PharmAust has made significant progress with its reformulation. In early 2016, the firm contracted Juniper Pharma Services[10] to reformulate the drug into capsules. However, the pill burden remained high (at 1 capsule/kg, 20 capsules for a large dog) and the capsule retained its bitter taste. To overcome these issues, the company contracted BRI Pharmaceutical Research in 2017 with the aims of improving taste and increasing the dosing concentration of MPL adjusted for bioavailability by tenfold relative to the previously tested formulation. In October 2018 the company reported that with BRI Pharmaceutical Research, it has achieved better than expected outcomes through micronization[11], a process that can deliver monepantel in a tablet while also potentially improving palatability. The company reported it reached blood levels in healthy Beagle dogs, sufficient to give anticancer activity with one tablet[12]. PharmAust is now on track to make GMP tablets to optimise its dosing levels in formal clinical trials[13]. In addition to BRI Pharmaceutical Research, the company is also contracting with Avista Pharma Solutions and Catalent to deliver a ready-to-use prototype of MPL for canine trials. Once the optimization of the final formulation is complete, the company plans to scale-up tablet manufacture for Phase I and II trials by Q4, 2018 (calendar year). A reformulated MPL that is more palatable has the potential for better patient compliance than the original drug.

PharmAust's option agreement with Elanco to develop MPL provides scale-up and commercial partnership opportunities. In April 2018, the firm signed an option agreement with Elanco[14] to develop MPL in dog cancers. Under the terms of the agreement, Elanco will supply MPL for dog cancer trials. In turn, PharmAust has granted Elanco the option to negotiate for an exclusive global royalty-bearing commercial license to utilize PharmAust's

[7] J Immunother Cancer. 2016;4:97.
[8] ILAR J. 2014;55(1):16-45.
[9] MPL has faced recruitment challenges in early-phase trials due to palatability issues.
[10] A UK-based contract manufacturing organizations.
[11] Micronization refers to a milling technique that grinds MPL into a fine powder that after further processing can then be packaged into capsules and tablets.
[12] Micronization is known to be able to improve the bioavailability of poorly soluble drugs – see Methods Find Exp Clin Pharmacol. 1998 Apr;20(3):211-5.
[13] In January 2018, PharmAust stated that micronization of MPL had met the company's dose and palatability requirements.
[14] Greenfield, In., NYSE: ELAN, www.elanco.com. Elanco did its IPO in 2018 and commenced trading on the NYSE on 20 September.

IP in the treatment of animal cancers. This option is stipulated to continue for no longer than 6 months after the receipt of the final report of the relevant canine trial. If Elanco chooses to exercise its option, the parties will enter into a negotiation period (not longer than 6 months) to agree on terms of license agreement. However, if Elanco chooses to forgo this option, PharmAust will be free to seek alternative partners for commercialization. The agreement provides a twofold benefit to PharmAust – it secures a stable supply of GMP-grade MPL that provides a scale-up opportunity ahead of planned trials in dog cancers, and it helps build relationship with a potential commercial partner.

THE ELANCO AGREEMENT PROVIDES OPPORTUNITY TO BUILD A RELATION WITH A POTENTIAL COMMERCIAL PARTNER

"For work related to canines we have an option agreement with Elanco, and for that related to humans we are looking for potential partners - it may be owners of Elanco that are currently divesting parts of Elanco, i.e., Eli Lilly." **– Dr. Roger Aston, CEO, PharmAust**

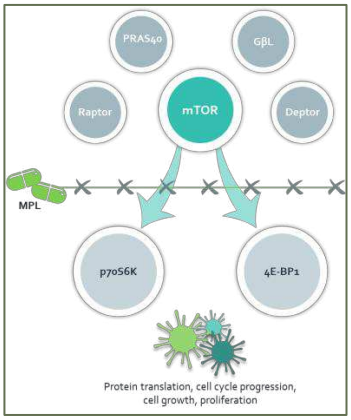
PharmAust's overall strategy is to sustain MPL through early-stage trials. It may choose to license it to a major pharma player in the future. PharmAust's overall strategy with MPL appears to revolve around sustaining the product through its early-stage clinical trials by overcoming palatability and pill burden issues (by collaborating with BRI Pharmaceutical Research) and sustaining funds and supply of GMP-grade MPL (through the option agreement with Elanco). Eventually, the company may choose to license the technology to pharma, veterinary, or biotechnology companies with the skills and resources to complete late-stage registration clinical trials, and manufacture and distribute products.

Monepantel is being studied in various cancers

MPL is an oral AAD compound that modulates the mTOR pathway in humans. Unlike chemotherapies, which treat cells by killing proliferating tumor cells (and some normal cells), MPL arrests cancer cells in dormancy and prevents their growth. In preclinical studies and early-phase trials, MPL has shown significant potential to suppress p70S6K and p-4E-BP1, both of which are downstream of the mTOR pathway and indicate aggressive cancer metastasis. Preclinical studies reveal that MPL suppresses the mTOR/p70S6K pathway in human ovarian cancer cells through autophagy[15]. High p70S6K is associated with poor outcomes (such as resistance to therapy, aggressive disease, poor prognosis, and high metastasis) in patients with colorectal, lung, ovarian, pancreatic, and hepatic cancers, while P-4E-BP1 expression in breast, colon, ovarian, and prostate tumors has been an indicator of malignancy[16]. Thus, MPL can be a potential treatment option in all these indications.

[15] Am J Cancer Res. 2014 Sep 6;4(5):558-71. eCollection 2014.
[16] Int J Mol Sci. 2012; 13(2): 1886–1918.

Figure 1: mTOR pathway and MPL activity



MPL MODULATES THE mTOR PATHWAY

***"There are 1st generation of mTOR inhibitors (including rapamycin) and 2nd generation of mTOR inhibitors. We believe we are in generation 3 or 4."* – Dr. Roger Aston, CEO, PharmAust**

MPL has shown clinical potential in canine cancers. However, low recruitment continues to be a challenge. PharmAust is evaluating MPL's potential in the treatment of canine cancers, both as a monotherapy and in combination with standard of care chemotherapy. In a Phase I/II safety and efficacy study, conducted in conjugation with Vet Oncology Consultants at the Animal Referral Hospital in Homebush in western Sydney, MPL suppressed cancer markers in 2 dogs and was well-tolerated by all dogs (n=11). Based on the encouraging results of this trial, the company moved on to explore the potential of MPL in an exploratory Phase II study in canines that had failed standard of care treatment. However, in December 2016, PharmAust reported that the recruitment to this trial was slower-than-expected due to a combination of 2 factors – many of the dogs available for treatment were too progressed to be acceptable, and palatability of the original liquid formulation was poor. Based on these observations, PharmAust decided to evaluate MPL in prior-stage canine patients and conducted a Phase II pilot study that evaluated MPL capsules (manufactured by Juniper Pharma Services) as a front-line therapy in dogs with B-cell lymphoma. The results were very encouraging, showing statistically significance for progression-free survival (stable disease induction) in 6 out of 7 dogs diagnosed with the disease, pointing towards the outstanding potential of MPL as a first-line therapy in dog lymphoma. However, poor palatability and suboptimal dosing issues remained. To resolve these, the company, as we have noted above, retained BRI Pharmaceutical l Research and expects to re-initiate clinical development of MPL in dog cancers with the palatable tablets that have now been developed. Besides its use as a monotherapy (in first-line and progressed settings), MPL is also being explored in combination with standards of care. In 2016, the company completed the treatment of 2 canine patients with MPL and carboplatin. Following significant anti-cancer activity observed in this trial, in March 2018, PharmAust collaborated with Dr. Doug Fairlie, a cancer researcher based in the Olivia Newton-John Cancer Research Institute (ONJCRI) in Melbourne, to identify drug combinations that improve MPL potency against various forms of cancer. The outcomes of this collaboration are expected to accelerate MPL's clinical development strategies in not only veterinary cancers but also human cancers.

"For Phase II trials in canines, we are planning to include a mix of dog populations requiring first-line and second-line therapy. If we get the right population of dogs, we only plan to evaluate 2 cancers in the beginning – lymphoma and basal cell carcinoma. Thereafter, we may progress to other aggressive but rarer forms of cancer, such as hemangiosarcoma." – **Dr. Roger Aston, CEO, PharmAust**

MPL has shown encouraging results in preclinical and early-phase human trials. However, palatability issues contributed to poor compliance and adverse events such as nausea. Preclinical studies in mice xenografts demonstrate potential use of MPL for reversal of chemoresistance – as a monotherapy, or in combination with standards of care for cancer treatment. In a few of these studies, brain cancer cells (glioma) resistant to temozolamide were killed by MPL, indicating its potential to be used in patients resistant to chemotherapy. In vitro studies also show that the treatment of ovarian cancer cells with MPL resulted in reduced cell viability, inhibition of cell proliferation, and suppression of colony formation. Furthermore, the drug decreased the growth of human ovarian tumor xenografts in immune-compromised mice, while it was well-tolerated and nontoxic to vital organs, as observed with untreated control animals[17]. Meanwhile, MPL has also shown preclinical activity in pancreatic and colorectal cancers as a monotherapy in mice xenografts. Based on these preclinical results, the company evaluated the anti-cancer activity of MPL in a Phase I 'first in man' trial. This was a Phase I dose evaluation study, carried out at Royal Adelaide Hospital in patients with solid tumors. All 6 patients who completed the trial displayed a reduction in p70S6K, and 4 out of 5 patients showed a reduction in p-4E-BP1. Moreover, MPL reported a better safety profile than many other anti-cancer drugs. However, poor palatability and suboptimal patient compliance were believed to be major contributors to AEs, arising from poor palatability, including nausea, vomiting, diarrhea, and decreased appetite. Recruitment stopped early in this trial[18]. Meanwhile, in its March 2016 quarterly update, PharmAust disclosed that it was evaluating plans to study MPL in a Phase II trial for esophageal cancers in patients from the UK and Australia. With the new, more palatable tablet formulation now available from BRI, evaluation of MPL's value in hard to treat cancers such as oesophageal cancer can now proceed.

MPL HAS SHOWN ENCOURAGING EARLY-PHASE CLINICAL TRIAL RESULTS

"We have patents on the synergy between MPL and chemotherapy. We can take a step further and look at a combination of immunotherapy with MPL." – **Dr. Roger Aston, CEO, PharmAust**

Early-phase clinical trials indicate a superior toxicity profile for MPL, compared with most competitors. Pfizer and Novartis already have marketed mTOR drugs. The market for mTOR inhibitors is dominated by Novartis and Pfizer with their 3 marketed drugs – Afinitor, Rapamune, and Torisel. Of these, Afinitor and Torisel are

[17] Am J Cancer Res. 2014 Sep 6;4(5):545-57. eCollection 2014.
[18] Trial ID ACTRN12614000612617 at ANZCTR.

marketed for different forms of cancer. For breast cancer, renal cell carcinoma, and neuroendocrine tumors, the most common adverse reactions[19] reported with the use of Afinitor – the most significant competitor to MPL – include stomatitis, infections, rash, fatigue, diarrhea, edema, abdominal pain, nausea, fever, asthenia, cough, headache, and decreased appetite. Compared to Afinitor, MPL seems to have shown a better toxicity profile in a Phase I/II trial. Moreover, unlike Rapamune and Afinitor, MPL is not an immunosuppressant and preserves the immune system of cancer patients, potentially an important factor in preventing tumor progression. Furthermore, Rapamune and Afinitor are massive molecules in size as compared with MPL which is typically produced via only a few steps in manufacturing. This evidence and activities highlight the potential of MPL to be able to successfully fight for a market share in the competitive mTOR space.

Table 1: Marketed mTOR Inhibitors

Drug Name	Company	Indications
Afinitor (everolimus)	Novartis	- Breast Cancer - Neuroendocrine Tumors - Renal Cell Carcinoma - Renal Angiomyolipoma - Tuberous Sclerosis Complex
Rapamune (sirolimus)	Pfizer	- Prophylaxis of Organ Rejection in Patients Receiving Renal Transplants - Lymphangioleiomyomatosis
Torisel (temsirolimus)	Pfizer	- Renal Cell Carcinoma

Pfizer, AstraZeneca, and Eli Lilly are evaluating their mTOR inhibitors in early-stage trials in cancers in which MPL may have an opportunity. Considering PharmAust's activity, the likely applications for MPL are ovarian, colorectal, pancreatic, and esophageal cancers[20]. An analysis of the pipeline of mTOR inhibitors in these cancer indications reveals that most drugs under development are studied in combination with other targeted therapies in early-stage trials. Moreover, most of these trials are expected to complete only after 2018, with the earliest launch estimated by H2 2026 in the US and the EU. MPL seems to be leading the pack, with Phase I/II studies already completed.

NOVARTIS, PFIZER, ASTRAZENECA, AND ELI LILLY CAN BE POTENTIAL THREATS

According to data from clinicaltrials.gov, most of the studies evaluating drugs used in esophageal cancer treatment are being conducted by academic institutions. Therefore, this indication seems to be untapped by major industry players and provides an attractive opportunity to PharmAust to become the 'first-to-market' with an mTOR inhibitor in esophageal cancer. However, it may face competition from major pharma players, including AstraZeneca, Pfizer, and Eli Lilly, in other relevant cancer indications.

[19] Adverse reactions are defined as adverse events with incidence ≥ 30%.
[20] These include indications in which PharmAust has reported some preclinical evidence or revealed plans to evaluate the drug such as colorectal cancer, pancreatic cancer, ovarian cancer, and esophageal cancer.

Table 2: Pipeline of mTOR Inhibitors in Relevant Cancer Indications[21]

Drug Name	Company	Indications	Clinical Phase	Estimated Launch Date[22]
AZD2014 (in combination with olaparib)	AstraZeneca	Multiple cancers, including ovarian cancer	Phase I/II	H2 2026 (both US and EU)
Gedatolisib (in combination with palbociclib)	Pfizer	Solid tumors, including pancreatic and colorectal cancers	Phase I	H2 2028 (both US and EU)
LY3023414 (monotherapy and/or chemotherapy, or targeted therapies)	Eli Lilly	Solid tumors, including colorectal cancer	Phase I	H1 2027 (US) and H2 2027 (EU)

MARKET OPPORTUNITY OF MPL IN CANCERS IS SIGNIFICANT

There is a strong market opportunity for MPL in human cancers. According to the WHO estimates, cancer is the second leading cause of death globally, and led to 8.8 million deaths in 2015. In the US alone, 1.73 million new cancer cases and 0.61 million deaths are expected to occur in 2018 (as per the American Cancer Society). Table 3 below outlines new cancer cases and deaths estimated by the American Cancer Society in 2017 and 2018 for the cancers relevant to PharmAust. The data suggests that colorectal cancer has the highest incidence rate, with comparably low estimated cancer deaths. This type of cancer may, therefore, provide a market opportunity to PharmAust.

Table 3: Estimated New Cancer Cases and Cancer Deaths in the US

Cancer Type	Estimated New Cancer Cases (US)		Percentage Change	Estimated Cancer Deaths (US)		Percentage Change
	2017E	2018E	Y-o-Y% Change	2017E	2018E	Y-o-Y% Change
Colorectal[23]	135,430	140,250	3.6	50,260	50,630	0.7
Esophageal	16,940	17,290	2.1	15,690	15,850	1.0
Ovarian	22,440	22,240	(0.9)	14,080	14,070	(0.1)
Pancreatic	53,670	55,440	3.3	43,090	44,330	2.9

"Our plan is to select 1-2 cancers. These cancers will be aggressive with short life expectancy because we are looking to block progression and see PFS as the endpoint." **– Dr. Roger Aston, CEO, PharmAust**

[21] The data is derived from clinicaltrials.gov and validated using PubMed, company websites, and other secondary research sources; only company-sponsored trials (excluding those for vaccine, risk prevention, etc.) with primary completion date in 2016 or later were considered for this analysis.
[22] Phase I/II drugs are considered to be in Phase II for estimated launch date calculation.
[23] Includes combined cancer incidence of colon and rectum cancer.

According to a 2011 analysis by the National Institutes of Health, medical expenditure on cancer in the US in 2020 is expected to rise at least by 27% over 2010 (US$ 158 billion vs. US$ 124.6 billion at constant incidence, survival, and cost). Meanwhile, as per a 2018 report by the IQVIA, global spending on cancer medicines continues to rise, with therapeutic and supportive care use growing from US$ 96 billion in 2013 to US$ 133 billion in 2017. Global spending may continue to grow and reach US$ 200 billion by 2022. Further, the report highlights that list prices of new cancer drugs at launch have risen steadily over the past decade, with the median annual cost of a new cancer drug launched in 2017 exceeding US$ 150,000 (almost doubling from US$ 79,000 in 2013). In a 2017 study published in *Plos One*, Tartari et. al. indicate that the average monthly cost of currently marketed mTOR inhibitors in cancer Afinitor and Torisel is US$ 7,000 and US$ 2,960, respectively[24]. This provides an opportunity for PharmAust to price MPL comparably or even higher, as no currently marketed products are being studied in cancer indications that PharmAust may venture into. However, this will be based on the assumption that it shows similar safety and efficacy profile in late-stage trials as well.

GLOBAL SPENDING ON CANCER DRUGS IS EXPECTED TO RISE

Table 4: Cost in US$ Billion

Cancer Type	US Cost of Cancer Care (US$ Billion)[25]		% Change
	2010	2020F	
Colorectal	14.14	17.41	23.1
Esophageal	1.33	1.76	32.3
Ovarian	5.12	6.03	17.8
Pancreatic	2.27	2.83	-24.7

Table 5: Average Monthly Cost of Marketed mTOR Inhibitors in Cancer

mTOR Inhibitors (Cancer)	Average Monthly Cost (US$)
Afinitor (everolimus)	7,000 (breast cancer)
Torisel (temsirolimus)	2,960 (RCC)

[24] PLoS One. 2017 Aug 22;12(8):e0183639. eCollection 2017.
[25] J Natl Cancer Inst. 2011 Jan 19; 103(2): 117–128.

Monepantel's payoff in animal health could be strong

The animal health market, especially the companion animal segment, is expected to continue to grow. The global veterinary drugs market is poised to grow at a 5.1% CAGR during 2016–2024. Estimated to be at US$17.2 billion in 2015, it is projected to reach US$26.7 billion in 2024. Growth is expected to directly correspond to a greater spending on companion animals. Moreover, it will likely be driven even further by improved surgical, therapeutic, and medical capabilities for companion animals that tend to increase their life-span. According to a 2018 report by Market Research Future, the companion animal segment of the animal health market is growing continuously and is expected to grow at a 9.6% CAGR during 2017–2023, reaching US$20 billion in 2023. It is anticipated that the market will be driven by an increase in the number of people that have pets (due to a rise in disposable income), the growing importance of healthcare and vaccination for animal owners, and government initiatives (e.g., 'One Health' initiative).

Dogs are among the most popular pets, followed by cats. In 2017, there were a total of 60.2 million households that own a pet dog and 47.1 million of those that own pet cats in the US. Moreover, an online survey conducted by Gfk involving 27,000 people across 22 countries in 2015 found that 56% of the world's inhabitants own at least 1 pet. In the US, during a pet's lifetime (10 years for dogs and 15 for cats) the median expenditure on medicines was estimated to be US$ 5,154 for a dog and US$ 5,325 for a cat in 2017[26]. Almost half the deaths of pets over 10 years of age are caused by cancer, and it is the most common cause of death in dogs. Out of the total pet dog population in the US, 6 million new cancer cases are diagnosed every year.

THE COMPANION ANIMALS SEGMENT IS EXPECTED TO CONTINUE TO GROW

Among the various types of cancers in dogs, canine lymphoma is the most common, accounting for 7–24% of all cancers in dogs. The minimal annual incidence rate of canine lymphoma is 13–114 per 100,000 dogs. Lymphoma can be diagnosed in dogs at any age, but middle-aged to older dogs are more prone to it, with an incidence rate increasing with age from 1.5 cases per 100,000 dogs for dogs <1 year of age to 84 per 100,000 for dogs >10 years. There are various options available for treating canine lymphoma in dogs, such as chemotherapy, antibody therapy, and transplantation (stem and bone marrow). Though chemotherapy is the most commonly used treatment as it is well-tolerated and causes few side effects, various factors compel companion animal owners to look for an alternate treatment. Chemotherapy may increase the quality of life but does not prolong lifespan; also, the response rate initially is high but reduces in later cycles as cancer cells start developing resistance to the treatment. There is an unmet need for therapies that can overcome the issues caused by traditional methods for treating cancer in companion animals; therefore, MPL may find a significant market opportunity in this segment.

The US market provides a lucrative investment opportunity in the companion animal segment. According to a 2013 report by Horspool, the global animal health market is consolidated, with the top 10 players controlling the majority of the market share[27]. In the US, 60% revenue of US Animal Health companies comes from companion animal products while the trend is the opposite in other markets. This indicates that the US market

[26] The Economic and Social Contributions of the Animal Health Industry, NDP Analytics, February 2018 (estimation by The Simple Dollar).
[27] Animal Health Markets and Opportunities: Companion Animal Landscape, Linda J.I. Horspool, Chapter 2.

offers lucrative opportunities for investment as pet owners are willing to spend more to ensure longer and healthier lives for their pets. Globally, over the past few years, the animal health industry has witnessed considerably high-value mergers and acquisitions between major industry players. Continuous acquisitions and large-scale investments are expected to continue to fuel the animal health market. The evolving focus of the animal health industry toward the companion health segment is expected to provide an opportunity to MPL for quickly entering the market.

Table 6: Major players in the Companion Animal Health Market

Company Name	FY 2017 Revenue (US $ billion)[28]	Overview
Bayer Animal Health	1.8	A business unit of Bayer, the company provides products to protect animals, including dogs, cats, and farm animals, including anti-infectives, pharmacological therapies, and farm hygiene therapies
Boehringer Ingelheim Animal Health	3.9	A business unit of Boehringer Ingelheim, the company develops vaccines, parasiticides, and pharmaceuticals for animal health
Ceva Sante Animale	1.3	This global animal health company offering products for companion animals, poultry, ruminants, and swine
Dechra Pharmaceuticals	0.5[29]	The company provides a range of product offerings for major therapeutic categories in the animal health segment, predominantly for companion animals
Elanco (formerly Eli Lilly Animal Health)	3.1	Elanco provides products and services for animal disease management and production efficiency, pet care, and the overall well-being of animals
Merck Animal Health	3.9	A business unit of Merck & Co., the company provides vaccines, anti-infective and antiparasitic drugs, fertility management products, pharmaceutical specialty products, technologies, and value-added programs, such as pet recovery services and livestock data management tools
Nutreco	1.2	Nutreco is a Netherlands-based producer of animal nutrition, fish feed, and processed meat products
Vetoquinol	0.4	A family-owned business, the company develops, manufactures, and markets veterinary medicines and non-medicinal products
Virbac	1.0 (56% from companion animals)	A French company, Virbac provides animal health products and services
Zoetis	5.3 (42% from companion animals)	The company develops and manufactures animal health medicines and vaccines, diagnostic products, genetic tests, biodevices, and services to meet the needs of veterinarians and the livestock farmers and companion animal owners they support

[28] All currency conversions are at US$ 1 = EUR 0.86362; US$ 1 =GBP 0.77834 of September 05, 2018
[29] As of FY 2018 ending in June 2018

THERE IS LIMITED COMPETITION IN THE DOG LYMPHOMA MARKET

Table 7: Major Deals in Animal Health (2016–2018)

Buyer Company	Target Company	Transaction Value (US$ million)	Date of Announcement	Overview of Target
Zoetis	Nexvet Biopharma	85.0	April 2017	Nexvet Biopharma is a biologic therapeutics company developing a pipeline of monoclonal antibodies for companion animals in pain and other therapeutic areas
Phibro Animal Health	MVP Laboratories	46.6	January 2016	MVP Laboratories, based in Nebraska, is a privately held developer, manufacturer, and marketer of livestock vaccines, vaccine adjuvants, and other products
Dechra Pharmaceuticals	Apex Laboratories	41.2	September 2016	Apex Laboratories is a private veterinary pharmaceutical company that develops branded nonproprietary prescription and other related companion animal products in Australia and New Zealand
Ascendis Health	Cipla Agrimed and Cipla Vet	28.6	March 2017	Cipla Agrimed manufactures veterinary pharmaceutical products for livestock and large animals, while Cipla Vet engages in manufacturing companion animal veterinary products
Dechra Pharmaceuticals	Brovel	6.0	January 2016	Brovel, based in Mexico, produces pharmaceutical veterinary products for livestock and pets
Huvepharma and Opportunity 2009	Biovet Joint Stock Company	5.8	January 2016	Biovet Joint Stock Company manufactures and markets medicated and nutritional feed additives, enzymes, bulk active substances, and pharmaceuticals for animal productivity and health globally
Swedencare	Biodistra	0.4	July 2016	Biodistra manufactures and markets natural additives for dogs and cats

MPL may face some competition from chemotherapies ahead of it in animal health market; however, only conditionally approved therapies exist in the dog lymphoma space. The market for chemotherapies in pet

cancers (majorly dogs and cats) is not very competitive, with only few drugs approved by the US FDA. In fact, there are no approved therapies for cats in the US. In 2016, the agency gave a conditional go-ahead to VetDC's Tanovea-CA1 in dog lymphoma that may pose a direct threat to PharmAust's MPL, which is still being evaluated in mid-stage trials. However, it is noteworthy that although VetDc is a potential threat to PharmAust, it has also not been granted a full approval yet. In the past, the US FDA has withdrawn conditional approval of 2 drugs with potential in dog cancers – AB Science's Kinavet-CA1 (granted in 2011 and withdrawn in 2015) and Oasmia Pharmaceutical's Paccal Vet-CA1 (granted in 2014 and withdrawn in 2017). Based on this data, the fate of Tanovea-CA1 approval is expected to become clearer in the next 3–4 years.

Table 8: Chemotherapies Marketed for Cancer in Dogs

Chemotherapy Name[30]	Company	Indications	Approval
Palladia (toceranib phosphate)	Zoetis	Mast Cell Tumors in Dogs	Granted US FDA approval in 2009
Tanovea-CA1 (rabacfosadine for injection)	VetDC	Lymphoma in Dogs	Granted US FDA conditional approval in 2016

PharmAust is growing Epichem

Epichem has a long history of providing synthetic and medicinal chemistry services. Epichem, a wholly owned subsidiary of PharmAust, has been delivering products and services related to synthetic and medicinal chemistry to global drug discovery and pharmaceutical companies since 2003. It has a highly skilled team of scientists – most of them have PhDs and extensive industry experience. Epichem offers a wide range of high purity reference standards for the pharmaceutical and agrochemical industries. These standards include impurities, degradants and metabolites of Active Pharmaceutical Ingredients (APIs) and excipients which are used during the drug manufacturing process. The collection includes hard-to-find degradant standards exclusive to Epichem. It has a global client base, serving companies across 32 countries.

THERE ARE STRONG DRIVERS TO SUPPORT EPICHEM'S GROWTH TRAJECTORY

PharmAust has been expanding Epichem's capacity to meet higher demand. Epichem has continued to grow since its inception and the existing laboratories, which were last expanded in 2015, were operating at full capacity as of December 2017. To meet current and future demand, the company further expanded its laboratory space by ~50% in July 2018.

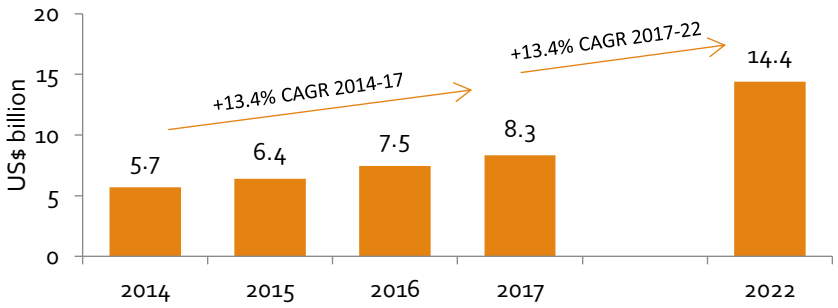
Epichem is well-positioned to meet the target revenue of A$6.2 million in FY2021. Epichem generated A$3.05 million revenue in 2017, an increase of 30% Y-o-Y. The increase was supported by growth across all business

[30] https://www.fda.gov/ForConsumers/ConsumerUpdates/ucm412208.htm

divisions of the firm – Epichem's Drug Discovery Services arm benefitted from a significant new customer based in the US, while growth in its Fine Chemicals & Technical Services business, which includes the high-margin reference standards (catalogue) business, was aided by Epichem's certification to the ISO9001 Quality Management System in 2016. In July 2018, Epichem gained accreditation from NATA (Australia's National Association of Testing Authorities) to ISO17034:2016, making it one of the first few companies in Australia to achieve this internationally recognized quality assurance standard. This enabled access to more global clients and drove substantial growth in the high-margin catalogs business. Given the expansion of lab facilities, extension of major contracts, and accreditations achieved, Epichem is well-positioned to accomplish its revenue target for FY2019 (A$4.3 million) and FY2021 (A$6.2 million).

The increasing inclination of major pharmaceutical companies toward outsourcing will benefit Epichem. To focus on its core competencies, increase the success rate of drug discovery programs, avoid regulatory hurdles, and decrease R&D costs, major pharma companies are increasingly outsourcing research activities to private contract research organizations. The global drug discovery service industry is anticipated to grow at an 11.6% CAGR to reach US$14.4 billion in 2022 from US$8.3 billion in 2017[31]. With pharmaceutical companies increasing their focus toward strategic outsourcing, we believe that Epichem can harness their scientific expertise to take advantage of growing demand for early- and late-stage R&D services.

Figure 2: Global Drug Discovery Service Industry



Rising R&D expenditure will further provide support to revenue growth. Continued high demand for advanced medicines is prompting many pharma companies to invest heavily in discovery and innovation, which will further sustain increased R&D activity. As per EvaluatePharma, global R&D spend by pharmaceutical companies is forecast to post a 3.1% CAGR between 2017 and 2024[32]. The R&D spend of the top 20 pharmaceutical companies is also anticipated to grow 2.6% over the same period. As high demand has created capacity issues for pharma companies, a large proportion of the expenditure is expected to go to the contract research organizations.

[31] Sourced from MarketsandMarkets Research.
[32] Sourced from EvaluatePharma.

Figure 3: Worldwide Pharmaceutical R&D Spend

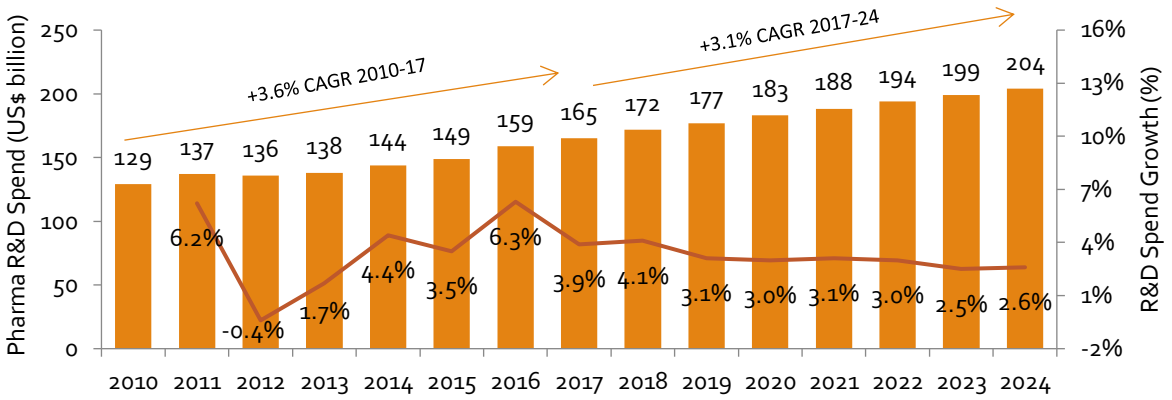


Table 9: Comparable companies for Epichem

Company name	Revenue (US$ m)	Description
Horizon Discovery (Cambridge, UK)	49	The firm provides genetic screening platforms; cell lines for drug manufacturing; and human genomic reference standards for labs, research centers, and manufacturers.
Selvita (Krakow, Poland)	30	The firm offers drug discovery services primarily in the area of oncology. Its most advanced R&D program SEL24, a dual PIM/FLT3 kinase inhibitor, is currently in Phase I/II trials in acute myeloid leukemia (AML) patients and was licensed to Menarini Group. The company's second-most advanced program is SEL120 – a small molecule inhibitor of CDK8, with potential use in lymphoma, colorectal cancer, and breast cancer.
Bioanalytical Systems (West Lafayette, IN)	23	It provides drug discovery services and analytical equipment for the pharmaceutical and biotechnology industries. Under its contract research services segment, the firm offers screening and pharmacological testing, formulation development, preclinical safety testing, regulatory compliance, and quality control testing services.
hVIVO (London, UK)	15	The company is developing an analytical platform to accelerate drug discovery and development in the areas of respiratory and infectious diseases. It also offers laboratory-based research solutions and biomarker discovery services to pharmaceutical and biotechnology companies.

Table 10: More comparable companies for Epichem

Company name	Revenue (US$ m)	Description
Orgenesis (Germantown, MD)	10	The firm is a contract development and manufacturing services provider in the regenerative medicine space. It serves pharmaceutical and biotech companies, as well as research institutions and hospitals involved in cell therapy. Orgenesis is also developing its own proprietary cell therapies.
1nKemia IUCT (Barcelona, Spain)	6	The company offers contract manufacturing and consulting services for industries such as chemical, pharmaceutical, biotechnological, cosmetic, and nutraceutical.
Collagen Solutions (London, UK)	5	The company develops medical-grade collagen biomaterials – which have applications in research, medical devices, and regenerative medicine domains. It also provides contract manufacturing services for collagen-based products.
Proteome Sciences (London, UK)	5	The company provides contract research services for identification, validation, and application of protein biomarkers – primarily focused on neurological, oncology, and cardiovascular conditions.

Valuing PharmAust

We valued PharmAust on a probability-weighted DCF basis. We value PharmAust at $0.10 base case and $0.21 optimistic case using a probability-weighted DCF approach. Our target price of $0.15 sits at around the midpoint of our valuation range. We valued only two aspects of the PharmAust story – Monepantel and Epichem.

General assumptions.

- **Discount rate.** We used a WACC of ~13%, appropriate in our view for a 'Medium' risk rating[33];
- **Probability of success.** For Monepantel in dogs, 50%. For Monepantel in humans, 20%. The latter number reflects the historic probabilities of success for a small molecule drug for human use in Phase 2. The former reflects the relatively lower risk profile of drugs for veterinary use where the treated subject is not part of a human food chain[34];

[33] For a relevant discount rate, we use varying WACCs depending on the risk for Life Science companies. We start with an RFR of the Australian ten year bond rate and an ungeared beta of 1.1 but use a variable MRP of 7.5%-11.5% (7.5% for 'medium risk' companies, 9.5% for 'high risk' companies and 11.5% for 'speculative' companies). We regard Life Science companies with existing businesses, or who have enough capital to reach the market with their products, as 'Medium' risk. Companies that have small revenue streams from marketed products but that are still potentially in need of capital are 'High' risk. Everything else is 'Speculative'.
[34] Clin Pharmacol Ther. 2010 Mar;87(3):272-7. Epub 2010 Feb 3.

- **Time horizon**. We used a 14-year time horizon in our DCFs followed by a terminal value;
- **Currency**. We assume the AUD/USD exchange converges on 0.7 over a three-year period from now.
- **Capital.** Purely for valuation purposes, we assume a further $10m is raised at $0.04 cents per share. PharmAust's previous funding round in December 2017 raised A$1.87 at $0.045 per share.
- **Commercial life of future products.** We assume that a product enjoys 15 years of commercial exclusivity, after which sales erode due to generic competition[35].

Table 11: Our valuation of PharmAust

	Base	Optim.
Monepantel veterinary (A$m)	11.5	38.5
Monepantel human (A$m)	7.9	36.5
Epichem	6.4	11.1
Total programme value	25.8	86.1
Value of tax losses	13.3	13.3
Corporate overhead	-9.7	-9.7
Cash now (A$m)	1.9	1.9
Cash to be raised (A$m)	10.0	10.0
Option exercises (A$m)	7.8	7.8
Total value (A$m)	49.1	109.4
Total diluted shares (million)	513.3	513.3
Value per share	$0.096	$0.213
Valuation midpoint	$0.155	
Share price now (A$ per share)	$0.040	
Upside to midpoint	286.3%	

Valuing Monepantel. To value Monepantel, we assumed payoffs from two future licensing transactions, one for veterinary use and one for human use. We estimated, for each of these potential future licenses, a base case and an optimistic case for the following elements:

- Level of expenditure required prior to a licensing deal;
- Timing of a prospective licensing deal;
- Level of upfronts in the deal (in US$);
- Level of milestones in the deal (in US$) – we assume that the probability of receiving those milestones declined evenly over time. We weighted the dollar value of milestones towards completion of Phase 2 and 3 as well as including some sales milestones.

[35] While patent protection for a drug is notionally 20 years, patent term extension in the US only covers that part of clinical programme after the filing of an IND. This reduces the exclusivity window by a few years. For large companies marketing blockbuster drugs, the window is around 15-16 years. Consider the Roche/Genentech cancer drug Herceptin. It gained FDA approval in September 1998 and enjoyed peak sales in 2014, for a 16-year window. Going further back in time, Amgen gained FDA approval for Epogen in June 1989. Its peak sales year was 2004, another 16-year window.

We also, estimated, for each license, a base case and an optimistic case for the following elements:

- Date of product launch in the US;
- Date of product launch for the Rest of the World (RoW);
- Level of royalties, as a percentage of net sales;
- The level of sales (in US$) to be achieved in the US at year five post launch;
- The level of sales (in US$) to be achieved in the RoW at year five post launch;
- The growth rate of sales in both the US and the RoW between years 6 and 14;
- The percentage of the US and RoW markets still held by the product when it goes generic;
- The terminal growth rate of the product franchise.

The parameters for each license were as follows:

	Monepantel dog project	
	Base case	**Optimistic case**
PAA investment required (AUDm)	3	1
License date	2021	2020
License upfront (USDm)	5	10
License milestones (USDm)	15	30
Royalty rate	10.0%	15.0%
Earliest approval	2025	2024
Peak sales (USDm)	100	200

	Monepantel human project	
	Base case	**Optimistic case**
PAA investment required (AUDm)	10	5
License date	2022	2021
License upfront (USDm)	10	20
License milestones (USDm)	30	50
Royalty rate	7.0%	11.0%
Earliest approval	2027	2026
Peak sales (USDm)	400	600

Valuing Epichem. For Epichem we assumed that Martine Keenan and her team can gradually build revenue to over A$5m by FY22, at which point profit before tax is just north of A$1m.This is conservative because Epichem believes that it can make >A$6m revenue by FY21, but reflects the fact that, historically, the business has grown slowly. From FY22, we developed base and optimistic case DCF models in which we assumed

- Revenue by year 15 of of ~A$7m (base case) to A$9m (optimistic case)

- 60-70% gross margins in 2022, alongside SG&A expenses equal to 30-35% of sales. We assume both COGS and SG&A decline by 0.1%-0.2% of revenue annually from 2022;
- Capex of 3% to 5% of revenue;
- A terminal growth rate of 3.0% to 5%
- Terminal margins of 25.0% for both base and optimistic case.

Re-rating PharmAust

We see various factors helping to re-rate PharmAust to our target price:

- New contract wins by Epichem;
- Exercise of the Elanco option;
- Further pre-clinical data on Monepantel in human cancers;
- Commencement of the human Phase 2 studies with Monepantel;
- More data on the effectiveness of Monepantel in canine cancers.

PharmAust's solid management team

The current top management has extensive sector experience and the ability to enhance shareholder value.

PHARMAUST HAS A SEASONED MANAGEMENT TEAM WITH A SUCCESSFUL TRACK RECORD

Executive Chairman and acting CEO **Dr. Roger Aston** has >20 years of experience in the pharmaceutical and healthcare industries. During his career, he has closely worked with start-ups and major pharmaceutical companies. Aston has held several executive and nonexecutive board positions in prominent private and publicly listed biotechnology companies – such as Pitney Pharmaceuticals, Mayne Pharma and the QinetiQ company pSivida. He is experienced in overseeing product registration activities with the US FDA and the EU; establishing and implementing guidelines and operating procedures for manufacturing and clinical trials; negotiating global license agreements; and organizing fundraising activities. Aston has been the firm's acting CEO since the retirement of Dr. Richard Hopkins in May 2018.

CSO **Dr. Richard Mollard** holds >20 years of experience in the pharmaceutical sector. He has held several scientific positions in Australia, France, and the US while working with University Louis Pasteur/ IGBMC, Bristol-Myers Squibb, University of Michigan, Eli Lilly, and Monash University. In Australia Mollard has been in charge of business development and technical due diligence for various ASX-listed companies – such as Agenix, Immuron, and Regeneus. He has founded several biotech start-up companies in which he held executive positions. Prior to joining PharmAust as CSO in March 2017, Mollard worked as a consultant with the company for 2 years and played a vital role in preparing and designing regulatory and clinical documents for PharmAust's canine and human trials.

Dr. Martine Keenan, previously Head of Discovery Services, was appointed Epichem's CEO in April 2018. She has been with Epichem since 2008 and has a strong know-how of the business. Keenan has >20 years' experience in drug discovery and has held a medicinal chemistry position in the Neuroscience division of Eli Lily.

PharmAust's current board, which includes Dr. Aston, is experienced and has various skills required for building a successful life sciences company:

PHARMAUST HAS A HIGHLY SKILLED AND EXPERIENCED BOARD

- **Robert Bishop** has been Executive Director at PharmAust since October 2013 and holds >30 years' experience in the corporate finance and equity capital markets. He previously worked in London and Sydney as a lawyer and an investment banker.
- **Sam Wright** has worked in the biotech and healthcare industry for >20 years and is experienced in the administration of ASX-listed companies, corporate governance, and corporate finance. He joined PharmAust in 2006 as Financial Controller and was later appointed Company Secretary in August 2007. He has been a Non-Executive Director since October 2008.
- **Neville Bassett**, Chairman of the Perth broking house Westar Capital, brings corporate skills[36].

PharmAust's **Advisory Committee** comprises three opinion leaders in the veterinary oncology space - **Dr Claire Cannon** of Werribee, Vic[37], **Dr Christian Schirvel** of Lyon, France[38] and **Dr Barbara Kitchell** of Albuquerque, NM.

Appendix I – A PharmAust glossary

Adverse Event – Any untoward medical occurrence in a patient/clinical investigation subject administered a pharmaceutical product.

Aminoacetonitrile Derivatives – A class of synthetic compounds that display high activity against gastro-intestinal nematodes. These derivatives cause spastic paralysis to and rapid expulsion of nematodes from the host.

Anthelminthic Drug – A drug that acts against internal parasites in order to expel them from the host's body.

Autophagy – A physiological process that involves destruction of damaged cells and formulation of new cells.

Bioavailability – The extent and rate at which a drug/metabolite enters systemic circulation, and thus accesses the site of action.

Biomarker – A natural molecule, gene, or characteristic used as an indicator of a biological state, especially to detect the presence or severity of a disease.

[36] Basset, who joined the PharmAust board in October 2018, replaced Dr. Wayne Best, currentl Chairman of Epichem. Best has >35 years of experience in the synthetic and medicinal chemistry, and biotechnology domains. He also founded Epichem in 2003.
[37] For a recent paper originating from her time at the University of Minnesota College of Veterinary Medicine see J Small Anim Pract. 2018 Mar;59(3):147-153. Epub 2017 Oct 13.
[38] Previously Head of Business Development and Licensing at Elanco.

Cancer Markers – A biomarker found in blood, urine, or body tissue that can be elevated by the presence of one or more types of cancers.

Canine – Dogs and dog-like animals, including various species of foxes, jackals, and wolves.

Cell proliferation – The process that results in an increase in the number of cells in the body. It is determined by the balance between cell division and cell loss through cell death/differentiation. Typically, cell proliferation increases in tumors.

Chemoresistance – The resistance of a cell to the action of any drug/chemical.

Chemotherapy – Drugs that stop the growth of cancer cells, either by killing them or by restricting cell division.

Clinical Trial – A type of research study that tests how well a new medical approach is working in humans.

CNS Disease – A neurological disorder that affects the function and structure of the brain/spinal cord, hence adversely impacting the Central Nervous System (CNS).

Collagen – The main structural protein found in skin and other connective tissue.

Cyclin-dependent Kinase (CDK) – A family of protein kinases, which function as central regulators of the cell cycle and transcription.

Dementia – A group of brain disorders that seriously affect a patient's ability to carry out daily activities.

Dose Escalation Study – Studies wherein subjects are enrolled in cohorts in which the drug is administered in an incremental fashion. Whether or not the study goes further to a higher dose depends on the assessment of the previous dose.

Enzyme – A protein that helps speed up biochemical reactions in the body. Enzymes generally have the suffix 'ase' in their name.

Exploratory Trial – Clinical trials that seek to identify, at an early stage of development, those drug molecules that show optimal/adequate pharmacodynamic or pharmacokinetic characteristics in humans.

FLT3 Kinase – A class III receptor tyrosine kinase.

Front-line/First-line Therapy – A treatment regimen, also called primary treatment, typically accepted by the medical establishment for the initial treatment of a given type and stage of cancer.

Gene – The basic physical and functional unit of heredity.

Immunotherapy – A type of treatment that boosts the body's natural defenses to fight cancer.

In vitro – Data obtained through tests conducted outside a living organism.

In vivo – Data obtained through tests conducted on live organisms, including animal models and humans.

Kinase – An enzyme that catalyzes the transfer of phosphate groups from high-energy, phosphate-donating molecules to specific substrates.

Lymphoma – A type of cancer that affects white blood cells (WBCs) or lymphocytes.

Malignancy – A disease in which a tumor invades adjacent normal cells though the lymph/blood system.

Metastatic cancer – A type of cancer that spreads from its point of origin to different body parts.

Monotherapy – A therapy that uses 1 type of treatment, such as a single drug, to treat a disease/condition.

mTOR – A serine/threonine protein kinase encoded by the mTOR gene in humans.

Mucolytic – A drug that reduces the thickness and stickiness of mucus (sputum) so it is easier to cough up. It helps relieve respiratory difficulties.

Neurodegenerative Disease – It is an umbrella term used for describing a range of conditions primarily affecting the neurons in the human brain.

Oncogenesis – The formation of a cancer, whereby normal cells are transformed into cancer cells.

Oncology – A branch of medicine that deals with the prevention, diagnosis, and treatment of tumors/cancer.

p-4E-BP1 – A binding protein and a member of the family of repressor proteins. It is a substrate of the mTOR signaling pathway.

p70S6K – A protein kinase that is encoded with the RPS6KB1 gene in humans. It leads to G1 cell cycle progression and cell growth.

Palatability – The pleasant/agreeable taste of food or drug.

Periodontal Disease – A gum disease caused by dental plaque, which results in pathological inflammation of the gum and periodontal tissue surrounding the teeth.

Phase I/II Trial – A study that tests the safety, side effects, best dose, and timing of a new treatment in humans. In Phase II, patients usually receive the highest dose of treatment that did not cause harmful side effects during Phase I of the clinical trial.

Pilot Trial – A small-scale version of the main study.

PIM Kinase –Proteins that play a vital role in cell cycle regulation. An increased PIM kinase expression is associated with malignant subtypes of leukemia, lymphoma, and a number of solid tumors, including pancreatic, colorectal, and esophageal cancers.

Preclinical Studies – Research that uses animals to find out if a drug, procedure, or treatment is likely to be useful.

Prognosis – The likely course of a medical condition.

Progressive Supranuclear Palsy – An uncommon brain disorder that causes serious problems with walking, balance, and eye movements.

Psychotropic – Relating to or denoting drugs that affect a person's mental state.

Repurposing – The identification of a new use/application of a product.

Rheumatoid Arthritis – An autoimmune disease that primarily affects the joints, making them swollen and painful.

Small Molecule – A drug that is able to enter cells easily because of its low molecular weight. It is different from drugs that have a large weight, such as monoclonal antibodies.

Solid Tumor – An abnormal mass of tissue that usually does not contain cysts or liquid areas – e.g., sarcomas, carcinomas, and lymphomas. Leukemias (cancers of the blood) generally do not form solid tumors.

Standard of Care – Treatment that is accepted by medical experts as a proper course of action for a certain type of disease, and widely used by healthcare professionals.

Tumor – An abnormal mass of tissue that is formed when cells divide more than they should or do not die when they should.

Vascular Endothelial Growth Factor (VEGF) – It is a signal protein produced by cells that stimulates the formation of blood vessels.

Xenograft – A process where a tissue is taken from 1 species and grafted onto a different species.

Appendix II – PharmAust's core intellectual property

PharmAust's core Intellectual property is covered by five patent families, all assigned to its subsidiary Pitney Pharmaceuticals. These include the following:

Kinase inhibitors for the treatment of cancer, WO/2013/138863; priority date March 23, 2012; invented by David Morris.

- Covers the use of AADs in the treatment of cancers (such as ovarian, breast, prostate, and mesothelioma). Anticancer activity and low toxicity of AADs, such as MPL, allow more flexible dosing regimens for cancer therapy, with limited side effects.
- Was granted in the US as patent number 9,308,193 in April 2016, and in Europe as 2,817,286 in June 2018.
- Was granted in Australia as patent number2,016,204,389 in May 2018 and 2,013,234,869 in October 2016.
- Was granted and published as patent number 1,04,364,232 in May 2017 in China.
- Additionally, patent applications were granted in Hong Kong and published as patent numbers 1,205,500 and 1,223,832 in December 2015 and August 2017, respectively.
- Was also granted and published in Japan as patent number 6,165,231 in May 2015.

Compounds for the treatment of mTOR pathway-related diseases, WO/2014/022879; priority date August 6, 2012; invented by Mohammad Hossein Pourgholami, David Morris, and Roger Aston.

- Pertains to the effective action of AADs in the treatment of mTOR pathway-related diseases (other than cancer).

- Was granted in the US as patent number 9,790,176 in October 2017, and in Europe as EP 2,880,014 in May 2017.
- Was granted in Australia as patent number 2,016,234,924 in July 2017 and as number 2,013,302,209 in January 2017.
- Was granted in China as patent number 1,04,837,812 in September 2017.
- Was granted in Hong Kong and published as patent number 1,205,502 in December 2015

Anticancer agent comprising aminoacetonitrile compound as active ingredient, WO/2015/037747; priority date September 13, 2013; invented by Nobuharu Andoh, Osamu Sanpei, Tetsuo Toga, David Morris, Roger Aston, Koji Tanaka, and Tomokazu Hino.

- Covers PharmAust's MPL that comprises an aminoacetonitrile-based anticancer agent that is safe to use, with reduced side effects, and has superior anticancer activity.
- Was granted in the US as patent number 9,907,778 in March 2018.

Pharmaceutical combinations for the treatment of cancer, WO/2015/061832; priority date November 1, 2013; invented by David Morris, Mohammad Hossein Pourgholami, and Roger Aston.

- Focuses on a pharma composition that contains aminoacetonitrile derivatives (AADs) – e.g., MPL – and an anticancer compound, such as doxorubicin, cisplatin, gemcitabine, and 5-fluorouracil. The combination was found to dramatically enhance the efficacy of anticancer compounds.
- Was granted in the US as patent number 9,833,431 in December 2017.

Anticancer agent comprising aminoacetonitrile compound as active ingredient, WO/2016/137010; priority date February 24, 2015; invented by Nobuharu Andoh, Osamu Sanpei, Tetsuo Toga, David Morris, Roger Aston, Koji Tanaka, and Tomokazu Hino.

- Covers an aminoacetonitrile compound or its pharmacologically acceptable salt that shows cell growth inhibitory action and anticancer activity.

Appendix III – Capital structure summary

		% of fully diluted	Note
Ordinary shares, ASX Code PAA (million)	199.0	75.6%	
Unlisted options (million)	57.5	21.9%	Average exercise price 13.5 cents, average expiry date 26-Jun-2020
Performance rights (million)	6.8	2.6%	
Fully diluted shares	263.3		

Current market cap:	A$8 million (US$5.7 million)
Current share price	$0.040
Twelve month range	$0.034 - $0.074
Average turnover per day (last three months)	1.21 million

Appendix IV – Major shareholders

PharmAust currently has the following substantial shareholders:

- Hybrid Holdings Pty Ltd (Graham Darcy of Perth) (5.5%);
- Dr. Roger Aston (5.2%);

Appendix V – Papers relevant to PharmAust

Prier JE and Brodey RS (1963), *Canine neoplasia. a prototype for human cancer study.* Bull World Health Organ. 1963;29:331-44 (full text available for free online).

- This paper reviews knowledge of spontaneous neoplasms in the dog, including the prevalence of certain types of canine tumors, and comparisons between the occurrence of similar neoplasms in humans

Dickerson et. al. (2002), *Potential to target dysregulated interleukin-2 receptor expression in canine lymphoid and hematopoietic malignancies as a model for human cancer.* J Immunother. 2002 Jan-Feb;25 (1):36-45.

- This paper provides evidence that canine lymphoma and leukemia can be used as suitable models to refine therapeutic approaches targeting the interleukin-2 receptor (IL-2R)

Ostrander EA and Comstock KE. (2004), *The domestic dog genome.* Curr Biol. 2004 Feb 3; 14 (3):R98-9 (full text available for free online).

- This paper provides canine genome map and DNA sequence that offer considerable opportunities for understanding the genetic regulation that accounts for the greatest extremes of natural variation

Phillips et. al. (2006), *Mutation analysis of PIK3CA and PIK3CB in esophageal cancer and Barrett's esophagus.* Int J Cancer. 2006 May 15;118(10):2644-6 (full text available for free online).

- This paper provides evidence that PIK3CA mutations are seen in esophageal tumors cells

Paoloni M and Khanna C. (2008), *Translation of new cancer treatments from pet dogs to humans.* Nat Rev Cancer. 2008 Feb;8(2):147-56.

- This paper reviews the potential opportunity of studying similarities between naturally occurring cancers in pet dogs and humans to identify genes associated with cancer, study environmental risk factors, understand tumor biology and progression, and develop novel cancer therapeutics

Trinh et. al. (2009), *The rationale for mTOR inhibition in epithelial ovarian cancer.* Expert Opin Investig Drugs. 2009 Dec;18(12):1885-91.

- This review discusses the rationale for the use of mTOR inhibitors in ovarian cancer and summarizes the available preclinical findings

Shigaki et. al. (2013), *PIK3CA mutation is associated with a favorable prognosis among patients with curatively resected esophageal squamous cell carcinoma.* Clin Cancer Res. 2013 May 1; 19(9):2451-9. Epub 2013 Mar 26 (full text available for free online).

- This paper provides evidence that PIK3CA mutations in esophageal squamous cell carcinoma are associated with longer survival, suggesting their role as a prognostic biomarker

Alvarez CE (2014), *Naturally occurring cancers in dogs: insights for translational genetics and medicine.* ILAR J. 2014;55(1):16-45 (full text available for free online).

- This paper provides evidence that companion dog models are genetically more like humans, share environmental exposures with their owners, and suffer from the same diseases as humans.

Bahrami et. al. (2014), *Monepantel induces autophagy in human ovarian cancer cells through disruption of the mTOR/p70S6K signalling pathway.* Am J Cancer Res. 2014 Sep 6; 4(5):558-71. eCollection 2014 (full text available for free online).

- This paper provides evidence that MPL triggers autophagy through the deactivation of the mTOR/p70S6K signaling pathway

Bahrami et. al. (2014), *Anticancer properties of novel aminoacetonitrile derivative monepantel (ADD 1566) in pre-clinical models of human ovarian cancer.* Am J Cancer Res. 2014 Sep 6; 4(5):558-71. eCollection 2014 (full text available for free online).

- This paper provides preclinical evidence that treatment of epithelial ovarian cancer cells with MPL results in reduced cell viability, inhibition of cell proliferation, and suppression of colony formation

Li et. al. (2014), *PI3K/AKT/mTOR signaling pathway as a therapeutic target for ovarian cancer.* Arch Gynecol Obstet. 2014 Dec; 290(6):1067-78. Epub 2014 Aug 3.

- This paper provides an overview of the PI3K pathway and its pathological aberrations reported in ovarian cancer. It also discusses PI3K pathway inhibitors currently under development and the challenges they face in future clinical utility

Li et. al. (2014), *Suppression of esophageal tumor growth and chemoresistance by directly targeting the PI3K/AKT pathway.* Oncotarget. 2014 Nov 30;5(22):11576-87 (full text available for free online).

- This paper provides evidence that PI3K/AKT is a valid therapeutic target in esophageal cancer patients and suggests the use of PI3K/AKT inhibitors, in conjunction with conventional chemotherapy, as a potentially useful therapeutic strategy for such patients

Cheaib et. al. (2015), *The PI3K/Akt/mTOR pathway in ovarian cancer: therapeutic opportunities and challenges.* Chin J Cancer. 2015 Jan;34(1):4-16 (full text available for free online).

- This paper discusses the relevance of the PI3K pathway in ovarian cancer, provides a review of novel PI3K inhibitors currently in clinical trials, and addresses the challenges of drug resistance and predictive biomarkers

Sapareto et. al. (2015), *Point/Counterpoint. Spontaneous tumors in pets are an excellent translational model for human cancers.* Med Phys. 2015 Nov;42(11):6127-9 (full text available for free online).

- This paper debates the use of spontaneous tumors in pets as a translational model for human cancers

Shang et. al. (2018), *Downregulation of BIRC5 inhibits the migration and invasion of esophageal cancer cells by interacting with the PI3K/Akt signaling pathway.* Oncol Lett. 2018 Sep;16(3):3373-3379. Epub 2018 Jun 18 (full text available for free online).

- This paper provides evidence that BIRC5 is able to inhibit the migration and invasion of tumor cells, and regulate the expression of angiogenesis-associated factors

Tan et. al. (2018), *Tim-4 promotes the growth of colorectal cancer by activating angiogenesis and recruiting tumor-associated macrophages via the PI3K/AKT/mTOR signaling pathway.* Cancer Lett. 2018 Aug 14; S0304-3835(18)30524-X. Epub ahead of print.

- This paper presents evidence to show that Tim-4 is upregulated in CRC tissues, compared with neighboring normal tissues, and activates PI3K/AKT/mTOR signaling in CRC cells

Xiong et. al. (2018), *TRIM44 promotes human esophageal cancer progression via the AKT/mTOR pathway.* Cancer Sci. 2018 Aug 10. Epub ahead of print (full text available for free online)

- This paper offers evidence showing that TRIM44 plays a vital role in human esophageal cancer development and may be a novel prognostic indicator for human esophageal cancer patients after curative resection

Xu et. al. (2018), *IGF2 induces CD133 expression in esophageal cancer cells to promote cancer stemness.* Cancer Lett. 2018 Jul 1;425:88-100. Epub 2018 Mar 29.

- This paper provides evidence that knockdown of IGF2 or treatment with PI3K/AKT inhibitors markedly restricted the ability of CD133-positive esophageal squamous cell carcinoma cells to self-renew, resist chemotherapeutic drugs, and form tumors cells

Appendix VI – Companies to watch

Company	Location	Code	Market cap (USDm)	Web
Kindred Biosciences	San Francisco, Ca.	Nasdaq: KIN	487	www.kindredbio.com
Humanigen	Brisbane, Ca.	OTCQB: HGEN	66	www.humanigen.com
IntelGenx	Saint-Laurent, Qc	TSX-V: IGX	57	www.intelgenx.com
Theranexus	Lyon, France	Alternext: ALTHX	56	www.theranexus.com
Ampio Pharmaceuticals	Greenwood Village, Co.	Nasdaq: AMPE	49	www.ampiopharma.com
SELLAS Life Sciences	New York, NY	Nasdaq: SLS	35	www.sellaslifesciences.com
Cyclacel Pharmaceuticals	Berkeley Heights, NJ	Nasdaq: CYCC	16	www.cyclacel.com
Therapeutic Solutions Internatio	Oceanside, Ca.	OTCBB: TSOI	8	www.therapeuticsolutionsint.com
Race Oncology	Melbourne, Australia	ASX: RAC	8	www.raceoncology.com
EastGate Biotech	Toronto, On.	OTCBB: ETBI	5	www.eastgatebiotech.com

Ampio Pharmaceuticals. The biopharmaceutical company develops drugs for the treatment of metabolic diseases, eye diseases, inflammation, kidney diseases, and CNS diseases. It is developing Optina, a repurposed oral drug with an established human safety profile, for the treatment of diabetic macular edema.

Cyclacel Pharmaceuticals. The clinical stage company develops oral therapies for the treatment of cancer and other life-threatening diseases. Cyclacel's oral cyclin dependent kinase (CDK) inhibitor Seliciclib (which is currently in clinical development to treat certain cancers) is being repurposed to treat rheumatoid arthritis in patients who are unresponsive to existing treatments.

EastGate Biotech. The company focuses on developing formulations of natural compounds and pharmaceutical products, primarily for the treatment of type 2 diabetes. It partnered with Genome Pharmaceuticals to expand the indication of its liquid insulin mouth rinse solution to include the Alzheimer's disease.

Humanigen. The firm repositions and develops its monoclonal antibodies for the treatment of oncology and immunotherapy. Its lead asset Lenzilumab is being developed as a potential medicine for chimeric antigen receptor T cell (CAR-T) therapy, which is leveraged for cancer treatment.

IntelGenx. The company develops novel oral immediate-release and controlled-release products. It is working to repurpose Montelukast, a medicine marketed for the treatment of asthma, to treat neurodegenerative diseases – such as mild cognitive impairment, dementia, and Alzheimer's disease.

Kindred Biosciences. The firm focuses on repositioning existing human drugs for animals such as dogs, cats, and horses. It has only 1 approved drug Mirataz, a transdermal medication to manage weight loss in cats. Currently, Kindred is developing medication for controlling fever, dermatitis, anemia, metabolic syndrome, and bowel disease.

Race Oncology. The company is repurposing Bisantrene, a chemotherapy drug, for the treatment of acute myeloid leukemia (AML). The drug was approved for AML in France in 1990, but disappeared after a series of large pharmaceutical mergers. Race Oncology aims to complete the drug's clinical development and obtain approval from the US FDA.

SELLAS Life Sciences. The company is a late-stage biopharmaceutical company focused on the development of immunotherapies for various cancer indications. SELLAS partnered with Catalent Pharma Solutions to repurpose Zolpidem, a drug currently being used to treat insomnia, for curing Parkinson's disease and the orphan indication Progressive Supranuclear Palsy (PSP).

Therapeutic Solutions International. The firm focuses on immune modulation therapies to treat cancers and periodontal disease and improve maternal and fetal health. It develops drugs that are unlikely to cause toxicity by focusing on naturally occurring products or repositioning of drugs that are considered safe. In 2017, the company filed a patent covering a repurposing of Mifepristone for use in stimulation of T and NK cells, which are crucial to sustain anti-cancer immunity.

Theranexus. The company leverages its patented technology to improve the efficacy of psychotropic drugs, which are approved and available in the market, by combining them with a glial cell modulator. It develops drugs for the treatment of CNS disorders. Its drug THN201 is used for curing neurocognitive disorders related to Alzheimer's disease.

Risks related to PharmAust

Risks specific to PharmAust. We see several major risks for PharmAust as a company and as a listed stock:

- **Clinical Risk**. There is a possibility that late-stage trials (Phase II/III) are unable to show the required efficacy profile or report an intolerable safety concern with MPL. The company has already reported AEs in early-stage trials due to the drug's pill burden and palatability issues. There is a considerable risk of these issues arising again if reformulation of MPL does not lead to expected results.
- **Delayed Market Entry Risk**. The company is already witnessing multiple recruitment challenges in MPL trials that may impede the time-to-market if not addressed immediately.
- **Regulatory Risk**. The anticancer drug industry is highly regulated and there is a risk that unfavorable regulatory decisions may slow or stop the progress of PharmAust's products.
- **Reimbursement Risk.** As PharmAust is developing its lead candidate, MPL, for the treatment of cancers, the drug is expected to be priced at a premium (in line with the cost of other cancer therapies). This will likely increase the company's dependency on third-party payers, such as private insurance companies. If these payers and government health administration authorities do not reimburse or limit the amount of reimbursement, it may lead to a fall in PharmAust's sales and revenue.
- **Manufacturing Risk.** Though the company has signed an option agreement with Elanco to secure supply of GMP-grade MPL during its clinical development in dog cancers, a failure to sustain it in the commercialization phase can impact revenue.
- **IP Risk.** Failure to obtain new patents or protect issued patents may negatively impact PharmAust share price.
- **Capital Funding Risk.** There is a risk that the company may not be able to raise funds for further growth and investment in new technologies.
- **Competition Risk.** MPL is expected to compete with mTOR inhibitors manufactured by pharmaceutical giants such as Novartis and Pfizer. Most of these companies are better financed and have more advanced capabilities across the drug development value chain.

Risks related to pre-revenue Life Science companies in general.

- The stocks of biotechnology and medical device companies without revenue streams from product sales or ongoing service revenue should always be regarded as speculative in character.
- As most biotechnology and medical device companies listed on the Australian Securities Exchange fit this description, the term 'speculative' can reasonably be applied to the entire sector.
- The fact that the intellectual property base of most biotechnology and medical devices lies in science not generally regarded as accessible to the layman adds to the risk with which the sector ought to be regarded.

Caveat emptor. Investors are advised to be cognizant of the abovementioned specific and general risks before buying any the stock of any biotechnology or medical device stock mentioned on this report, including PharmAust.

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