

Investor Newsletter

November 2018

Dear investors,

The past few months has been a period of intense activity for the entire Kazia team, and it has been very gratifying to see the hard work begin to pay off.

The company now has four human trials underway; two phase II studies and one phase I study with GDC-0084, and one phase I study with Cantrixil. Two of the GDC-0084 studies are led by, and largely funded by, the hospitals that are running them, which happen to be among the leading cancer research hospitals in the world. All of these studies are being performed under the oversight of the US FDA.

One of the most difficult challenges for most small companies in our field lies in winning the interest of top tier clinicians. With GDC-0084, we have had the opposite problem – there are many more brain cancer experts wanting to be involved with the drug than we have capacity to support at this stage.

This is a remarkable position to find ourselves in, and it is the product of tenacious hard work by the Kazia team. In this newsletter we have tried to provide a flavour of the projects that are ongoing.

It has been hugely encouraging to see that newfound scientific credibility reflected for the first time in the interest of professional life sciences investors. Last month, we completed a share placement of \$3.4M, primarily to sector-specialist funds. Although the capital this brings in is important, the validation it provides to our company is no less important. Kazia has, at last, become a serious contender in the complex and challenging landscape of global drug development.

We have said for the last twelve months that any financing activities would be mindful of the interests of existing shareholders. To that end, we have acted in a restrained way, raising just what is needed to support the programs through their milestones without bringing unnecessary dilution. We have also offered existing shareholders the ability to participate on the same terms via a Share Purchase Plan (SPP). Although the SPP is not critical from a financial perspective, we felt it important that all shareholders have the same opportunity as our new institutional investors.

This is an excellent time to be a Kazia shareholder, with world-class clinical trials providing multiple data read-outs over the coming twelve months, any one of which could be transformative for the company. We are grateful as always for the ongoing support of our shareholders, and look forward to sharing our continued progress.

Best wishes,

Dr James Garner

News Summary

Highlights from our recent company announcements:

- 23 October 2018: Share Purchase Plan offer documentation released
- 22 October 2018: Kazia enters clinical collab' with Dana-Farber Cancer Institute
- 18 October 2018: Kazia raises \$3.4m with support from sector specialist investors
- 10 October 2018: Kazia's Cantrixil completes Part A of phase I study
- 3 October 2018: Kazia enters clinical collab' with St Jude Children's Hospital

Upcoming Events

- 16 November 2018: GDC-0084 poster presentation at Society for Neuro-Oncology in New Orleans
- 8 November 2018: Kazia's AGM: From 10am at K&L Gates: L31, 1 O'Connell St, Sydney

Visit the Kazia website homepage to follow future events.

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Collaborating to create new opportunities for GDC-0084

Kazia recently announced collaborations with two leading US-based research hospitals to explore GDC-0084 in other forms of brain cancer. St Jude Children's Research Hospital is conducting a phase I human trial in DIPG, an aggressive form of childhood brain cancer, and Dana-Farber Cancer Institute will be running a phase II human trial in breast cancer brain metastases, which is breast cancer that has spread to the brain.

Kazia's Dr Jeremy Simpson explained the difference between these studies and Kazia's ongoing phase II study in glioblastoma, the most common and most aggressive form of brain cancer.

"The glioblastoma study has been designed and is being run and funded by Kazia. This is almost always the way that new drugs get to market. However, when a drug represents cutting-edge science, researchers and clinicians sometimes ask to explore it in other disease areas. These 'investigator-initiated' studies can be a great way for a company to obtain valuable new data. The fact that these studies are largely funded by the hospitals themselves demonstrates just what an exciting drug candidate GDC-0084 has become."



Dana-Farber Cancer Institute in Boston

Dana-Farber Cancer Institute (DFCI) is considered one of the top cancer hospitals in the United States, and sees approximately 300,000 patients per annum. It is closely tied to Harvard Medical School, and is described as a Comprehensive Cancer Center by the US National Cancer Institute.

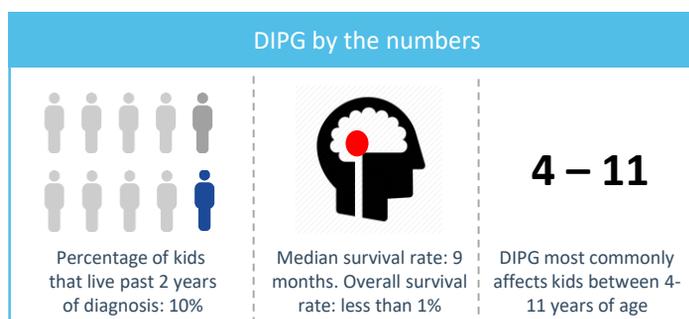
Dr Pablo Leone is the Principal Investigator for the Kazia collaboration at DFCI, and he describes the scientific rationale for the study.

"We know that when breast cancer spreads to the brain, it becomes very difficult to treat. Unfortunately, this ultimately occurs in 10-25% of this group of patients. There is good data suggesting that a PI3K inhibitor may provide benefit, and GDC-0084 is of particular interest because it is able to cross the blood-brain barrier, which prevents many drugs from

acting in the brain. Our study is designed to understand the potential of the drug in this disease, and we are excited to be moving it forward."

In October, Novartis, a Swiss pharmaceutical company, presented data at the European Society for Medical Oncology meeting that showed good results for their PI3K inhibitor in breast cancer that has remained in the breast.

The phase I study at St Jude Children's Research Hospital will explore GDC-0084 in DIPG, an aggressive form of childhood brain cancer.



DIPG remains a very challenging disease, with no drug treatment to date showing convincing evidence of benefit. Dr Chris Tinkle at St Jude outlined why GDC-0084 may be of interest.

"GDC-0084 is of interest as a potential therapy for diffuse midline glioma given its potent activity against a core signalling pathway that is frequently altered in these tumors and its ability to cross the blood-brain barrier and target these deep-seated tumors."

The two collaborations leave GDC-0084 with a rich and robust portfolio of three ongoing clinical studies, two in phase II and one in phase I.

"We always knew that GDC-0084 would be of interest beyond glioblastoma," explained Kazia CEO, Dr James Garner. "Although glioblastoma is the fastest, most dependable path to market for the drug, we see huge potential for it in other forms of brain cancer. These two collaborations with some of the best hospitals in their respective fields will help us to understand that potential. It is a really positive reflection on the drug that we have clinicians of this calibre, at such prestigious hospitals, keen to work on the drug."

"We have had a great deal of interest from other researchers and clinicians who want to work with GDC-0084, and we are working with them to help think through the best approaches. Our ultimate goal is to provide benefit to the largest number of patients, but the data these studies generate will also be of value in our discussions with the FDA, and with potential partners."

Interview with Dr Matt Dun

We wanted to share the story of Dr Matt Dun, a leading cancer researcher based at Newcastle's Hunter Medical Research Institute. Dr Dun's daughter Josie, 2, was diagnosed with the aggressive childhood brain stem cancer Diffuse Intrinsic Pontine Glioma (DIPG) in February of this year.

Josie's illness was diagnosed after Dr Dun was called at work by Josie's day care as she was displaying uncharacteristically clumsy behaviour.

Following his daughter's diagnosis, Dr Dun immediately began to develop his own research program particularly focused on predicting the progression of DIPG in its early stages, and testing new drug therapies in a bid to improve survival. Dr Dun has raised a staggering \$200,000 (AUD) to fund his work. Kazia's brain cancer drug GDC-0084 is one of the therapies Dr Dun has been working with.

Why did you become a cancer researcher?

After an early career in the Royal Australian Navy as a Submariner, I completed a PhD and have been investigating how reoccurring gene mutations in cancer control how cancer cells communicates, and whether these altered signalling pathways may be used as drug targets to disrupt their growth and survival. A lot of my work has been in haematological malignancies, but I have added a significant focus on DIPG since Josie's diagnosis.

How did you hear about GDC-0084?

A colleague of mine is friends with Dr Jeremy Simpson, the Clinical Program Director for GDC-0084, and she had seen phase I data on the drug presented, noting particularly that it was a PI3-kinase inhibitor. I don't know how she knew that PI3-kinase was playing a role in Josie's tumour, but she was right, Josie has an activating mutations to PIK3CA, the gene coding for catalytic subunit p110alpha of PI3K catalytic subunit, (amongst other mutations) but I suppose she had a bit of a guess. That's what sparked my interest straight away - most kinase inhibitors don't cross the blood brain barrier, so they're ineffective in treating brain cancers, but GDC-0084 does. So I reached out to Dr Simpson.

What work have you undertaken so far with GDC-0084?

We've undertaken over six months of work, carrying out cytotoxicity assays and cell growth and proliferation assays in six DIPG cell lines and five glioblastoma cell lines. We've performed detailed phosphoproteomic investigations to characterise the pathways inhibited downstream of PI3K and directly compared the response of DIPG cells with therapies used in the clinic (Josie) to inhibit this oncogenic pathway. The literature shows that this pathway is probably the most overactivated in DIPG as not only are PI3K mutations common, but each of the growth factor receptors that control PI3K activation are overexpressed.

How do these early data compare to other treatment approaches you have examined?

We've seen that the DIPG cells are even more sensitive



to the drug than the glioblastoma cells, so it's looking very promising. The concentration of the drug required to kill DIPG cells is half of what is required to elicit the same level of cytotoxicity as say mTOR inhibitors that are listed on the PBS, and commonly prescribed to patients with PI3K aberrations.

What's next in your work with GDC-0084?

We'll move into preclinical modelling of DIPG in January.

Could Josie be a candidate for a GDC-0084 treatment one day?

Absolutely. We are reminded every day of the urgency of our research, and we are all fighting as hard as we can to keep Josie around long enough for us to be able try this if the preclinical studies show as much promise as the in vitro or laboratory testing.

Glioblastoma Update

In October, Kazia provided a progress update on its phase IIa study of GDC-0084 in glioblastoma, which is progressing very well.

All seven hospitals that are participating are open to recruitment, and the first cohort of patients are fully enrolled and receiving the drug. The first part of the study is aiming to determine the optimal dose for patients with newly-diagnosed glioblastoma, and this should be completed in the first quarter of calendar 2019.

Given the rapid pace of recruitment, the company has accelerated the manufacture of a second batch of capsules for use in the study. GDC-0084 is taken by mouth once a day.

A poster presentation on the glioblastoma study will be presented at the Society for Neuro-Oncology Annual Meeting in New Orleans on 16 November 2018.

Cantrixil MTD reported, trial moves to **Phase I, Part B**

In early October, Kazia was delighted to announce the successful completion of Part A, the dose escalation component, of our phase I study of Cantrixil in ovarian cancer.

Part A of the study was designed to test that Cantrixil was safe and could be tolerated by patients. It also set out to determine the maximally tolerated dose (MTD), which was determined to be 5 mg of Cantrixil for each kilogram of body weight.

The study will now move into Part B, a dose expansion cohort, which is designed to seek further preliminary evidence of efficacy. Part B will recruit 12 patients, all of whom are expected to be dosed at the MTD. Part B is expected to conclude in calendar 2019.

Kazia CEO, Dr James Garner, commented, “we are delighted with progress in the Cantrixil study. The first hurdle for any drug in development is safety, and so it is highly encouraging that we have achieved in Part A of the trial a dose for Cantrixil towards the upper end of the range that we set out to explore. The study will now immediately transition into Part B, which will provide important insights into the potential efficacy of Cantrixil, building on the preliminary data that was announced in June 2018.”

The interim data announced in June 2018 was covered by Ovarian Cancer News. [Read the coverage here.](#)

Recent media



Our CEO, Dr James Garner [was interviewed](#) by Morgans Financial's Senior Analyst, Scott Power about Kazia's clinical trials and upcoming milestones.



Finance News Network (FNN) [covered Kazia's](#) trial progress and coming milestones.



Our collaboration with Dana-Farber Cancer Research Institute was covered by [Onco'Zine](#), oncology network magazine and [Biotech Dispatch](#)

Learn about our Share Purchase Plan [read more](#)

Share Purchase Plan **now open**

In mid October, Kazia completed a placement of shares to high-quality sector-specialist institutional investors. This placement represented a powerful endorsement of both the quality of our pipeline and the work that has been done over the past several years to move it forward. We are delighted that such high calibre investors have invested.

Existing eligible shareholders are now being offered the same opportunity to invest, via a Share Purchase Plan (SPP) in recognition of their long-standing support. Those shareholders have the opportunity to purchase up to \$15,000 of new shares at a price of \$0.38 per share, without incurring costs for brokerage or other transaction fees.

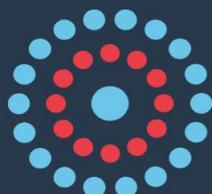
The next twelve months is a very exciting period for Kazia, with four high-impact data read-outs across the main GDC-0084 and Cantrixil programs. The funds raised in the placement will enable us to see through the phase IIa study of GDC-0084 and the phase I study of Cantrixil.

The SPP opened on 23 October and is expected to close on 16 November 2018.

The SPP booklet contains all information on the offer. All eligible shareholders will be mailed the booklet and personalised application forms.

Kazia Directors all intend to invest in the offer, and shareholders are encouraged to consider the opportunity strengthen their investment in the company.

For all the specifics on the SPP, please visit our website at kaziatherapeutics.com



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