

# Kazia Therapeutics

Pipeline update

## GDC-0084 Phase II underway

Pharma &amp; biotech

Kazia Therapeutics has initiated the dose optimization lead-in component of the Phase II trial of GDC-0084 in glioblastoma, with initial data expected in Q119. Initial data from the Cantrixil ovarian cancer Phase I are due shortly. In January Kazia received a ~5% shareholding in Noxopharm (current market value ~\$3m) in return for collaborative support of that company's lead program. We roll forward our DCF model and add in the Noxopharm shareholding, which increases our valuation to between \$56m and \$101m.

11 May 2018

**Price** **\$5.40**
**Market cap** **\$26m**

ADR/Ord conversion ratio 10/1

Net cash (\$m) at 31 December 2017 5.0

ADRs in issue 4.8m

ADR Code KZIA

ADR exchange NASDAQ

Underlying exchange ASX

Depository BNY

Year end	Revenue (US\$m)	PTP (US\$m)	EPADR (\$)	DPADR (\$)	P/E (x)	Gross Yield (%)
06/16	2.8	(8.8)	(2.16)	0.0	N/A	N/A
06/17	6.5	(8.3)	(1.73)	0.0	N/A	N/A
06/18e	10.0	(3.3)	(0.66)	0.0	N/A	N/A
06/19e	10.3	(5.5)	(1.10)	0.0	N/A	N/A

Note: Converted at A\$1/US\$0.76 for the table above and throughout the note.

## GDC-0084 Phase II lead-in underway

Kazia has initiated a Phase II study of its oral PI3K inhibitor GDC-0084 in recently diagnosed glioblastoma (GBM). Genentech's Phase I study of the drug was in sicker patients whose disease had relapsed after treatment, so Kazia's trial includes a lead-in component to test whether newly diagnosed patients can tolerate higher doses of the drug, before the randomized study begins. The open-label lead-in should provide an initial data readout in early 2019.

## GDC-0084 is targeting an unmet need in GBM

The trial will test GDC-0084 in GBM patients who have an unmethylated O6-methylguanine methyltransferase (MGMT) promotor. This subgroup, which represents ~61% of GBM patients, is known to obtain little benefit from standard temozolomide chemotherapy. The clear unmet need in this patient group could open access to accelerated approval pathways and allow approval of GDC-0084 as early as 2023.

## Phase I Cantrixil data this year

Kazia is expected to report the maximum tolerated dose (MTD) from the Phase I ovarian cancer study of Cantrixil in Q218. Potential efficacy signals from a 12-patient expansion cohort at the MTD are expected to readout later in 2018.

## Valuation: Increased to \$56-101m in two scenarios

We have increased our indicative valuation range to \$56-101m or \$11.10-20.16 per share (vs \$53-96m, \$10.88-19.89 per share), under either post-Phase III approval or accelerated approval scenarios for GDC-0084. The valuation changes reflect rolling forward our DCF model and adding in the Noxopharm shareholding. Kazia had \$5.0m cash at 31 December 2017, and received a \$3.0m R&D rebate in February. We forecast current cash will be sufficient to fund operations into FY19, by which time preliminary Cantrixil data are likely to read out. We estimate the company may require ~\$5m of additional funding in FY19, part of which could be secured against the Noxopharm shareholding.

## ADR share price performance



52-week high/low \$6.25 \$2.40

## Business description

Kazia Therapeutics is an ASX- and NASDAQ-listed biotechnology company. It is developing the PI3K/mTOR inhibitor GDC-0084 for brain cancer and Cantrixil for ovarian cancer. GDC-0084 was in-licensed from Genentech in 2016.

## Next events

Cantrixil Phase I MTD identified Q218

Cantrixil Phase I efficacy data H218

GDC-0084 initial data readout Q119

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**Kazia Therapeutics is a research client of Edison Investment Research Limited**

## Investment summary

### Company description: Two novel classes of anti-cancer drugs

Kazia Therapeutics (formerly Novogen) is an Australian biotechnology company focused on oncology drug development. It is listed on both the ASX (ASX:KZA) and NASDAQ (NASDAQ:KZIA). The company is developing two classes of anti-cancer compounds: GDC-0084, a PI3K inhibitor licensed from Genentech and a third-generation benzopyran drug Cantrixil. A Phase II trial of GDC-0084 in GBM is underway, and a Phase I trial of Cantrixil in ovarian cancer is expected to report preliminary data in the current quarter. Kazia has de-emphasized its anti-tropomyosin (ATM) drug discovery program, which is largely funded by a \$2.3m government grant. The company's product pipeline is summarized in Exhibit 1.

#### Exhibit 1: Kazia's product pipeline

Drug candidate	Indication	Stage	Next steps
GDC-0084	GBM	Phase II	Report initial data on GBM Phase II dose-optimization lead-in component Q119.
Cantrixil	Ovarian cancer	Phase I	Preliminary Phase I data Q218. Potential efficacy signals from expansion cohort Q418.
Anti-tropomyosin	TBA	Discovery	

Source: Edison Investment Research

### Valuation: \$56-101m, \$11.10-20.16 per share

We value Kazia between \$56m and \$101m. Our base case valuation of \$56m assumes that GDC-0084 could be approved in 2026 after a confirmatory pivotal trial. Our alternative valuation of \$101m is for a scenario where GDC-0084 seeks potential accelerated approval in 2023 after the current Phase II trial is completed. Our base case valuation is equal to \$11.10/ADR, or \$10.59/ADR after diluting for options and convertible notes. Our valuation is based on a risk-adjusted NPV analysis, which includes net cash and our forecasts for GDC-0084 and Cantrixil, with probability of success of 10-25% to reflect the stage of development of each product.

### Financials: Additional funds likely required in FY19

Kazia reported a profit of \$0.3m in H1 FY18 following the \$6m (mostly non-cash) legal settlement with Noxopharm. R&D expenditure for the period was \$3.6m, while SG&A (excluding D&A) was \$2.1m. We have increased forecast SG&A expenses (excluding D&A) by \$0.5m in both FY18 and FY19 but leave R&D expenditure unchanged at \$8.1m in FY18 and \$10.8m in FY19. Kazia had \$5.0m cash at 31 December 2017 and received a \$3.0m R&D rebate in February. We forecast current cash to be sufficient to fund operations into FY19, by which time preliminary Cantrixil data are likely to readout. We estimate the company may require ~\$5m of additional funding in FY19. Part of the FY19 funding requirement could be met by upfront payments if Cantrixil is out-licensed at the completion of the Phase I trial, while borrowing secured against the Noxopharm shareholding, or sale of the Noxopharm shares are another potential source of funds.

### Sensitivities

The key sensitivities for Kazia will be funding risk and the success of its lead drugs in clinical trials. A key question will be whether GDC-0084 works sufficiently well as a single agent in GBM to justify filing for accelerated approval, or whether a confirmatory Phase III trial (possibly in combination with radiotherapy or temozolomide) will be required for approval. In our base case scenario, we assume that a confirmatory trial will be required to prove efficacy of GDC-0084, delaying potential launch until 2026 versus 2023 under an accelerated approval scenario. While Kazia initiated the lead-in component of the Phase II study of GDC-0084 in GBM, it would require additional funds of ~\$20m to complete the trial, which could result in significant dilution of existing shareholders.

## Phase II trial of GDC-0084 in GBM underway

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Kazia initiated a Phase II clinical study of GDC-0084 in March in patients with recently diagnosed GBM, an aggressive brain cancer. It had in-licensed the drug from Genentech in October 2016. GDC-0084 is an orally administered small molecule phosphoinositide 3-kinase (PI3K) inhibitor that targets an important growth signaling pathway in cancer cells. The drug was specifically developed to cross the blood-brain barrier and target GBM, which is an aggressive brain cancer with poor patient survival and for which there are few effective therapies.

Genentech conducted a Phase I trial of GDC-0084 in patients with advanced disease, which confirmed it readily crosses the blood-brain barrier and led to dose-dependent inhibition of tumor growth. Seven of the eight patients treated at the maximum tolerated dose of 45mg/day demonstrated levels of drug in the bloodstream that were associated with significant inhibition of tumor growth in preclinical models.

### GBM: An aggressive brain cancer with few effective treatments

GBM is the most common and most aggressive primary malignant tumor of the brain and spinal cord. Approximately 11,500 patients are diagnosed with GBM each year in the US. GBM tumors are characterized by invasive and diffuse growth, which makes complete surgical removal difficult. Standard treatment for GBM entails surgical resection of the tumor followed by radiotherapy with concurrent chemotherapy with temozolomide (TMZ), followed by adjuvant chemotherapy with the same drug to treat the residual infiltrative component of the tumor. Despite this aggressive treatment the disease invariably returns, resulting in a five-year survival rate of only 5%.<sup>1</sup>

In February the US FDA granted GDC-0084 Orphan Drug Designation (ODD), which is accorded to drugs that are considered promising treatments for rare (orphan) diseases. ODD provides for a minimum of seven years of market exclusivity and provides opportunities for grant funding, protocol assistance and FDA fee waivers.

### GDC-0084 Phase II begins with a dose optimisation lead-in

Genentech's Phase I [study](#) identified the MTD of GDC-0084 as 45mg/kg. This was conducted in very sick patients with late-stage disease and rapidly growing tumors whose disease had progressed despite having received one or more previous treatments.

In contrast, Kazia's Phase II study will be conducted in newly diagnosed (first-line) patients who have undergone surgery to remove the bulk of the tumor and a course of chemoradiotherapy to further reduce the tumor burden. As these recently-diagnosed patients are expected to be in better overall health, Kazia is testing whether they are able to tolerate higher doses of GDC-0084 in a lead-in study before it moves on to the randomized stage of the trial. The open-label dose optimization lead-in will initially treat patients at 60mg/kg, the highest dose that Genentech tested in its study. Depending on the side effects observed, the dose could be either increased to 75mg/kg or decreased to 45mg/kg, the current MTD.

Once the MTD in first-line patients is identified, an expansion cohort of 10-12 patients will be treated at that dose. These patients will undergo intensive monitoring to better understand the pharmacokinetic and toxicity profile of the drug, including the effect on major organs including the heart.

Patient monitoring will also include pharmacodynamic studies to confirm that the drug is having the desired pharmacological effects. These studies will likely include FDG-PET magnetic resonance

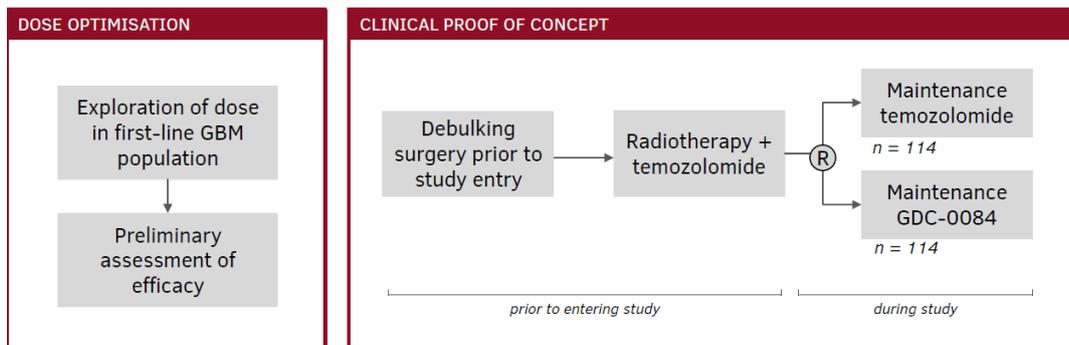
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<sup>1</sup> CBTRUS Statistical [Report](#): Primary Brain and Central Nervous System Tumors Diagnosed in the United States in 2008-2012. Ostrom et al *Neuro-Oncology* 17:iv1–iv62, 2015.

imaging studies to determine whether the drug is affecting tumor metabolic activity in patients who have detectable tumors.

In parallel with the expansion cohort, Kazia will also investigate the effectiveness of alternative dosing regimens such as dosing every second day or four days on then three days off. These regimens could be considered as alternatives to dose reduction in patients who experience unacceptable drug toxicity at the MTD when it is administered every day. The trial design shown in Exhibit 2 was finalized in consultation with Kazia’s clinical advisers after a constructive meeting with the US FDA in September. The randomized component of the Phase II study will compare maintenance therapy with GDC-0084 vs standard-of-care TMZ in recently diagnosed GBM patients who have undergone standard therapy of surgery to remove the bulk of the tumor and a course radiation therapy (XRT) combined with TMZ. After completing XRT, 228 patients will be randomized to receive maintenance therapy with either GDC-0084 or TMZ to treat residual tumor cells and delay recurrence of the disease. The study will target the 61% of GBM patients where tumor cells have an unmethylated MGMT promoter, as they receive only minimal benefit from treatment with TMZ and are in urgent need of more effective therapies.

**Exhibit 2: Revised GDC-0084 Phase II design includes a lead-in study**

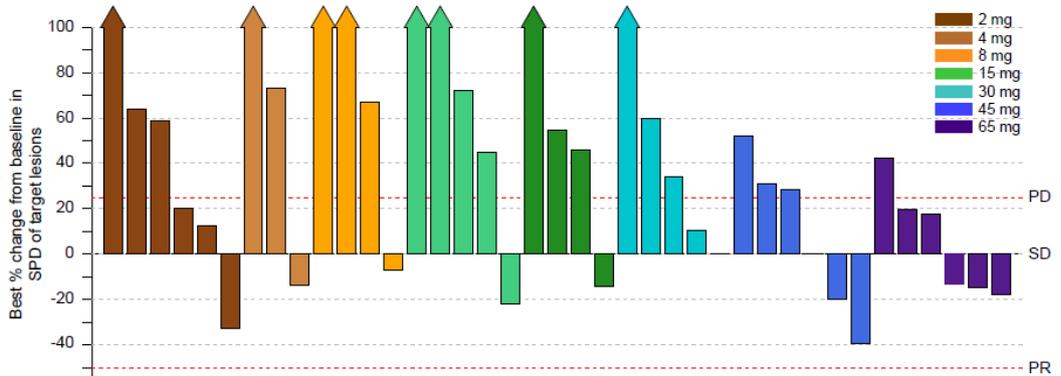


Source: Kazia 2017 AGM presentation

The open-label lead-in should provide an initial data readout in early 2019. As GDC-0084 is being used as an adjuvant therapy after the bulk of the tumor has been removed, many patients will not have measurable tumors at the start of the study, so they will not be able to be assessed for tumor response (shrinkage) according to the Response Assessment in Neuro-Oncology (RANO) criteria. Therefore, the key criteria will be progression free survival (PFS) and overall survival (OS). FDG-PET responses will be assessed to see whether they are able to predict PFS or OS.

Exhibit 3 summarizes the tumor responses for the patients in Genentech’s Phase I study of GDC-0084, grouped by dose cohort. Although none of the patients reached the 50% reduction in tumor size that would qualify as a partial response, a dose response in tumor growth was apparent, with much less tumor growth in patients treated at 45mg (the MTD) or higher doses. The dose response shown in Exhibit 3 provides encouragement that a higher dose of GDC-0084 may improve efficacy, which would increase the overall chance of success in the Phase II study. In addition to the reduction in tumor growth, 26% of patients showed a metabolic partial response on FDG-PET.

**Exhibit 3: GBM patients in Phase I trial showed a trend to better disease control at higher doses of GDC-0084**



Source: Wen et al 2016 [ASCO](#) poster. Note: Maximum tolerated dose was identified as 45mg (blue bars).

### Unmethylated MGMT promoter unlikely to affect GDC-0084

Kazia is trialing GDC-0084 as adjuvant therapy in newly diagnosed GBM patients where the promoter region of the MGMT gene is unmethylated. In a seminal study reported in 2005, Hegi et al<sup>2</sup> found that GBM patients with an unmethylated MGMT promoter received only minimal additional benefit when TMZ was added to radiotherapy in first-line treatment of newly diagnosed disease.

TMZ is an alkylating agent that adds a methyl group to purine bases of DNA, blocking DNA replication and leading to cell cycle arrest and apoptosis. MGMT can repair the DNA by removing the added methyl group, counteracting the cytotoxic effect of TMZ. Methylation of the MGMT promoter silences the gene, reducing MGMT activity in the cell and allowing TMZ to have its desired cytotoxic effect.

In contrast to TMZ, GDC-0084 blocks the PI3K signaling pathway, and does not interfere with DNA replication. Therefore, having an unmethylated MGMT promoter is not expected to interfere with the cancer-killing activity of GDC-0084. This is supported by preclinical studies performed by Genentech, which showed that GDC-0084 inhibited tumor growth in two different GBM tumor lines in which the MGMT promoter is unmethylated.

### Accelerated approval could see GDC-0084 launched in 2023

There are no effective therapies for GBM in those patients whose tumor cells have an unmethylated MGMT promoter. Therefore, if the Phase II trial shows a meaningful improvement in PFS or OS in these patients, there is a good prospect that it could be eligible to seek accelerated approval based on the Phase II data, rather than waiting for a standard approval after completing a confirmatory Phase III trial.

Because of this, we have evaluated timelines for an accelerated approval of GDC-0084 as well as approval following a Phase III trial, as we described in our [report](#) in December.

Exhibit 4 shows a potential scenario where GDC-0084 gains accelerated approval in GBM after demonstrating a statistically significant and clinically meaningful improvement in PFS, with a potential market launch in Q2 CY23.

2 Hegi et al *N Engl J Med* 2005;352(10):997-1003.

#### Exhibit 4: Assumed clinical trial and timeline for GDC-0084 accelerated approval

Calendar year	2018				2019				2020				2021				2022				2023				2024			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4
GDC-0084 accelerated approval GBM	Lead-in (1.25yr)				Phase II (2.5yr)				PFS				NDA, FDA approval				Launch Q2 CY23											

Source: Edison Investment Research

Under our second scenario, which assumes the results of the first Phase II trial indicate that GDC-0084 is efficacious against GBM, but that additional evidence from a second clinical trial is required before filing for approval, we forecast a potential market launch in Q4 CY26.

#### Exhibit 5: Assumed clinical trial and approval timeline for GDC-0084 under two-trial scenario

Calendar year	2018				2019				2020				2021				2022				2023				2024				2025				2026				2027			
	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4	Q1	Q2	Q3	Q4				
GDC-0084 accelerated approval GBM	Lead-in (1.25yr)				Phase II (2.5yr)				PFS																															
GDC-0084 second efficacy trial																	Phase III (3 Yr)								NDA, FDA approval				Launch Q4 CY26											

Source: Edison Investment Research

## Background: PI3K and history of GDC-0084

### PI3K is a promising target for GBM drug development

The PI3K signaling pathway plays a crucial role in cellular proliferation, metabolism, survival and apoptosis (programed cell death). PI3K signaling is initiated by receptor tyrosine kinases or G-protein coupled receptors located at the cell surface, and by some oncogenic proteins such as Ras.

The PI3K pathway is frequently over-activated in cancer. The over-activation can occur through a variety of mechanisms including mutation and amplification of genes in the pathway, or by loss of function of the tumor suppressor PTEN, which is a negative regulator of PI3K signaling. Abnormal PI3K signaling is associated with over 80% of cases of the GBM.<sup>3</sup>

The first approved cancer drugs that target the PI3K pathway were the rapamycin analogues everolimus and temsirolimus, which inhibit mTORC1. The PI3K inhibitor idelalisib (Zydelig, Gilead Sciences) was first approved by the FDA in 2014 and is approved to treat several types of leukemia and lymphoma. Idelalisib is a selective inhibitor of the delta isoform of PI3K (PI3K $\delta$ ). A second PI3K inhibitor copanlisib (Aliqopa, Bayer) was approved for treating lymphoma in September 2017. The approval of these two drugs provides validation for PI3K as a target for anticancer drug development.

In March 2016, Gilead halted six combination trials of idelalisib in newly diagnosed patients due to serious side effects including deaths from infections. Idelalisib inhibits PI3K $\delta$ , and this affects the immune system. In contrast, GDC-0084 most strongly inhibits PI3K $\alpha$  and also inhibits mTOR, and has not caused similar toxic side effects in clinical trials.

As far as we are aware, Kazia is the only company that is developing a PI3K inhibitor in GBM. Novartis has previously trialled its pan-PI3K inhibitor buparlisib (BKM120) in a 76-patient Phase II study in GBM in combination with Avastin. The tumor response rate in that study was 6% (1/17) in patients who had undergone prior Avastin therapy and 36% (18/50) in patients who had not previously been treated with Avastin. However, in a Phase III study in breast cancer the drug was found to be effective but was considered too toxic to warrant further development, and buparlisib is not listed in Novartis's current research pipeline. Novartis is instead studying the PI3K $\alpha$  inhibitor alpelisib (BYL719) in a Phase III study in breast cancer patients with mutations in the PIK3CA gene, but is not trialling alpelisib GBM.

<sup>3</sup> The Cancer Genome Atlas Research Network. Comprehensive genomic characterization defines human GBM genes and core pathways. Nature 2008, 455, 1061–1068.

## Cantrixil Phase I is expected to identify MTD in Q218

The Phase I study of Kazia's third-generation benzopyran drug Cantrixil in ovarian cancer, which began in December 2016, is expected to report the MTD in Q2 CY18. Once the MTD has been identified, an expansion cohort of 12 additional ovarian cancer patients will be treated at the MTD.

While the primary purpose of the trial is to demonstrate safety and tolerability, patients will also be assessed for tumor responses. A readout of potential efficacy signals is expected later in CY18. The US FDA has granted Cantrixil orphan drug status for ovarian cancer.

Cantrixil is being administered as an intraperitoneal (IP) therapy delivered directly into the abdominal cavity. IP administration delivers higher concentration of the drug to the site of the tumor for longer periods, and studies of advanced ovarian cancer patients have shown a survival benefit for IP delivery compared to intravenous administration of chemotherapy drugs.

Researchers at Yale University have shown that Cantrixil is active in a stringent, clinically relevant rodent model of human ovarian cancer. Cantrixil is the first drug to show uniformly high potency against the Yale library of ovarian cancer stem cells collected from tumors that had stopped responding to chemotherapy.

## High unmet need in ovarian cancer

Ovarian cancer accounts for 22,400 new cases and 14,100 deaths in the US each year, with a five-year survival rate of 47%. Worldwide there are an estimated 239,000 new cases and 152,000 deaths annually according to the International Agency for Research on Cancer with the highest rates coming from developed countries. The majority of those diagnosed already have distant metastases, which is associated with a 28.9% five-year survival rate (see Exhibit 6).

Exhibit 6: Ovarian cancer statistics		
Stage	% of cases	Five-year survival
Localized (confined to primary site)	15	92.5%
Regional (spread to regional lymph nodes)	20	73.0%
Distant (metastatic)	60	28.9%
Unknown	6	25.1%

Source: National Cancer Institute, Surveillance, Epidemiology and End Results Program

Patients who present with ovarian cancer are typically treated with surgery followed by a platinum based chemotherapy (such as paclitaxel and carboplatin). Unfortunately, around 70% of patients relapse in the first three years following therapy,<sup>4</sup> although this figure is expected to improve, especially among the 10% of ovarian cancer patients with BRCA mutations, with the approval of the PARP inhibitor niraparib by the FDA as a maintenance therapy. PARP inhibitors are also used in those with BRCA mutations in later lines of therapy.

The situation is dire for patients who are platinum refractory or who become platinum resistant (a condition that eventually occurs in all surviving platinum-sensitive patients following repeated platinum courses). The current standard of care for platinum resistant or refractory patients is either PEGylated lysosomal doxorubicin (FDA approved in 1999) or topotecan (FDA approved in 1996), both of which typically have shown a response rate of 10-15%, PFS of approximately 3.5 months and overall survival of 12 months in large trials.<sup>5</sup> This segment of the ovarian cancer population continues to be an unmet medical need and would likely be a key target for Cantrixil.

<sup>4</sup> Newly diagnosed and relapsed epithelial ovarian carcinoma, *Annals of Oncology* 24 (Supplement 6): vi24–vi32, 2013

<sup>5</sup> Luvero et al., Treatment options in recurrent ovarian cancer: latest evidence and clinical potential. *Therapeutic Advances in Medical Oncology*. 2014 Sep;6(5):229-39.

## **Kazia acquires Noxopharm shares in exchange for info and IP**

In December Kazia reached agreement with Noxopharm (ASX:NOX) to provide certain technical information to support the development of Noxopharm's lead program, and released Noxopharm from future claims by Kazia against the intellectual property associated with that program.

In exchange, Kazia was issued ~4.9% of Noxopharm's stock (5.3m shares) and 3m unlisted options over NOX stock that expire in January 2020 and are exercisable at A\$0.80 per share. The securities had an estimated market value of ~\$5m when they were issued in January, and the shares are subject to voluntary escrow until June.

The current CEO of Noxopharm, Dr Graham Kelly, was formerly chairman and CEO of Kazia (then known as Novogen), and resigned from the company in July 2015.

Based on the NOX share price of A\$0.83 on 4 May, the current market value of the 5.3m NOX shares is \$3.3m. Once the escrow agreement expires in June, Kazia would have the option of raising funds through the sale of the shareholding or through a loan secured against the shares.

## **Anti-tropomyosin program de-emphasised**

In February 2017, Kazia was awarded a grant of up to \$2.3m over three years by the Australian government to develop next-generation anti-tropomyosin (ATM) therapies for cancer treatment. Kazia is the lead partner in the collaboration that also involves the University of New South Wales and the privately held CRO, ICP Firefly. Kazia was expected to contribute \$0.8m and the University of New South Wales to contribute \$0.2m to funding the project.

For the time being Kazia has suspended investment into discovery research, including the next-generation ATM program, as it focuses its resources on GDC-0084 and Cantrixil.

## **Out-licensed preclinical benzopyran program to HBLs**

As part of its strategy to focus on clinical development programs, in November Kazia out-licensed its preclinical benzopyran and ad-het programs, including Trilexium, to Heaton-Brown Life Sciences (HBLs). Kazia retains a commercial interest in the preclinical assets, through a 10% shareholding in HBLs plus milestone and royalty payments linked to successful development. Kazia retains all rights relating to Cantrixil, and the agreement prevents the development of Trilexium as a therapy for ovarian cancer.

HBLs is a private company established by Dr Andrew Heaton and Dr David Brown, who are both former employees of Kazia and co-founders of the Triaxial technology that underpinned the third generation-benzopyran and ad-het programs. We do not know whether HBLs has the necessary financial resources to pursue clinical development of the benzopyran program.

## **Valuation**

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We have revised our valuation of Kazia to include the current market value of the Noxopharm shareholding, and have rolled forward the DCF model in time, including switching to end FY18e cash balance. When calculating value per share we have taken in to account the \$1.0m of shares that will be payable to the Glioblast vendors when the first patient is dosed in the Phase II trial.

We have valued GDC-0084 under two different development scenarios for GBM – in addition to our base case valuation, which assumes market launch in 2026 following completion of a Phase III trial, we have valued GDC-0084 assuming accelerated approval with a launch in 2023.

As a result of these changes, our base case valuation of Kazia has increased to \$56m (previously \$53m) or \$11.10/ADR undiluted (vs \$10.88 per ADR) and \$10.59/ADR after diluting for options and

convertible notes. Note that the per-ADR value does not account for the Glioblast milestone payment (\$1.0m of shares) potentially payable in FY21 on successful completion of Phase II. Kazia's primary listing is on the ASX under the code KZA; each NASDAQ-listed ADR represents 10 ordinary shares. Our undiluted base case valuation equals A\$1.46 per ASX-listed ordinary share at current exchange rates

Our base case valuation assumes a 40% likelihood that GDC-0084 is out-licensed to a marketing partner in 2021 after reporting positive PFS data from the Phase II trial, in a deal that includes \$20m upfront and \$120m in clinical and regulatory milestone payments. We also assume that Kazia pays a royalty of 10% of net sales to Genentech and that global sales for GBM reach \$1,050m in 2030.

Our valuation is based on a risk-adjusted discounted cash flow model. Our cash flow forecasts extend to 2035, but do not include any terminal valuation and apply a 12.5% discount rate. In calculating the diluted NPV/ADR, we assume that the \$0.4m remaining balance of the Triaxial convertible note is converted to 1.9m shares on completion of Phase II trials in 2021 (the \$1.1m convertible note was issued as part of the purchase of Triaxial and its third-generation benzopyran technology, \$0.7m was converted in H117, \$0.1m was extinguished as part of the settlement with Noxopharm).

Exhibit 7 shows our base case market assumptions for GDC-0084 and Cantrixil and the contribution of product royalties and milestone payments to the rNPV, which have not changed since our last note. We have offset the risk-adjusted trial cost against milestone revenue for each drug, rather than against royalty revenue. This understates the contribution of the milestone payments to the rNPV and overstates the contribution of royalties.

#### Exhibit 7: Kazia base case valuation (assumes confirmatory GDC-0084 pivotal trial required)

	Likelihood (%)	rNPV (\$m)	rNPV/ADR (\$)	Assumptions
GDC-0084; GBM	25%	12.2	2.43	Global peak sales* of \$1,050m from GBM (11,500 US cases/year, 61% unmethylated MGMT promoter, 80% penetration); pricing of \$50k. Global sales 2x US sales; launch 2026; assumes receives 15% royalty on sales, pays away 10% of royalty to Genentech.
GDC-0084; brain metastases in HER2+ breast cancer	20%	5.1	1.01	Global peak sales of \$570m (233,000 US breast cancer cases/year, 37% HER2+, 7% develop brain metastases, 50% penetration); pricing of \$50k. Global sales 2x US sales; launch 2026; assumes receives 15% royalty on sales, pays away 10% of royalty to Genentech.
Ovarian and other abdominal cancers: Cantrixil	10%	19.7	3.92	Global peak sales of \$680m from ovarian cancer (14,300 US deaths/year, 30% penetration) and bowel cancer (50,300 US deaths, 25% develop malignant ascites, 20% penetration); pricing of \$50k. Global sales 2x US sales; launch 2025; assumes receives 15% royalty on sales, pays away 5% of revenue to Yale.
GDC-0084 milestones		7.2	1.43	Assumes potential licensing upfronts and milestones total \$140m (\$127m net of payments to Glioblast and Genentech; \$38m after risk adjustment).
Cantrixil milestones		12.9	2.57	Assumes potential licensing upfronts and milestones total \$140m (\$23m after risk adjustment); assumes 5% of upfront and milestone payment paid away to Yale.
SG&A		-7.1	-1.42	
<b>Portfolio total</b>		<b>49.9</b>	<b>9.94</b>	
Noxopharm shares market value		3.1	0.62	
Cash (30 June 2018)		2.7	0.54	
<b>Enterprise total</b>		<b>55.7</b>	<b>11.10</b>	

Source: Edison Investment Research. Note: \*Peak sales in actual dollars in forecast year. We assume that the addressable markets grow at 4% per year. Launch dates listed are calendar years (in some cases the launch will be in the following financial year to the calendar year stated).

We have also valued Kazia under an alternative accelerated approval scenario for GDC-0084, which assumes a market launch in 2023 and that Kazia receives a higher 20% royalty rate and a larger \$40m upfront payment because the data are ready for filing, with other deal terms the same as for the post-Phase III approval base case scenario. Exhibit 8 shows that accelerated approval for GDC-0084 would increase our valuation for Kazia to \$101m (previously \$96m) or \$20.16/ADR (undiluted).

**Exhibit 8: Kazia valuation in GDC-0084 accelerated approval scenario**

	Likelihood (%)	rNPV (\$m)	rNPV/ADR (\$)	Assumptions
GDC-0084 – GBM	25%	45.8	9.13	As per Exhibit 7, except 2023 launch (vs 2026) and 20% gross royalty on sales (vs 15%).
GDC-0084 – brain metastases in HER2+ breast cancer	20%	10.1	2.02	As per Exhibit 7, except 20% gross royalty on sales (vs 15%).
GDC-0084 milestones		13.9	2.78	Assumes potential licensing upfronts and milestones total \$160m (\$147m net of payments to Glioblast and Genentech; \$48m after risk adjustment). Milestones received earlier than base case (final milestone in 2023 vs 2026).
<b>GDC-0084 total</b>		<b>69.9</b>	<b>13.93</b>	
Remainder of portfolio		25.4	5.07	
<b>Portfolio total</b>		<b>95.3</b>	<b>19.00</b>	
Noxopharm shares market value		3.1	0.62	
Cash (30 June 2018)		2.7	0.54	
<b>Enterprise total</b>		<b>101.1</b>	<b>20.16</b>	

Source: Edison Investment Research. Note: Launch dates listed are calendar years.

## Sensitivities

The key sensitivity for Kazia will be the success of its two lead drugs in clinical trials. A crucial question regarding GDC-0084 will be whether it works sufficiently well as a single agent in adjuvant therapy to justify accelerated approval. If it needs to be used concurrently with radiotherapy or with TMZ to deliver sufficient efficacy in GBM then one or more additional efficacy trials may be required, as outlined in our base case scenario, delaying potential launch until 2026 vs 2023 under an accelerated approval scenario. There is also a significant risk that GDC-0084 may not provide sufficient survival benefit to justify approval either as a single agent or combination therapy.

While Kazia has initiated the lead-in component of the Phase II study of GDC-0084 in GBM, we estimate that it would require additional funds of ~\$20m to complete the randomized Phase II component of the trial. This could result in significant dilution of existing shareholders given the current market capitalization of ~\$26m.

Our valuation includes revenues from the development of two drugs in four disease indications, as well as (risk-adjusted) upfront and milestone payments for two licensing deals. While each of these targeted indications is supported by the current preclinical efficacy studies and evidence of a dose response in the GDC-0084 Phase I trial, the company may not ultimately pursue development of the drugs for all of these indications. On the other hand, ongoing preclinical efficacy studies could identify additional disease indications that should be investigated in clinical trials. While we believe the drug development timelines used in our forecasts are achievable, at this early stage it is hard to accurately predict how long it will take to get the drugs to market.

## Financials

Kazia reported a profit of \$0.3m in H1 FY18 following the \$6m (mostly non-cash) legal settlement with Noxopharm. R&D expenditure for the period was \$3.6m, while SG&A (excluding D&A) was \$2.1m. We have revised our financial forecasts to include the Noxopharm settlement, and have increased SG&A (excluding D&A) by \$0.5m in both FY18 and FY19 to \$3.8m and \$3.7m, respectively). Our forecast R&D expenditure is unchanged at \$8.1m in FY18 and \$10.8m in FY19. Kazia had \$5.0m cash at 31 December 2017 and received an \$3.0m R&D rebate from the Australian government in February. We forecast cash to be sufficient to fund operations into FY19, by which time preliminary Cantrixil data are likely to readout. We estimate that the company may require ~\$5m of additional funding in FY19, which we show as illustrative long-term debt. Part of the FY19 funding requirement could be met by upfront payments if Cantrixil is out-licensed at the completion of the Phase I trial, while borrowing secured against the Noxopharm shareholding, or

sale of the Noxopharm shares are other potential sources of funds. Note that we include unrisks clinical trial costs in our financial forecasts to show the potential funding requirement if the clinical trial program is conducted in line with our expectations (trial costs risk-adjusted for NPV calculation).

**Exhibit 9: Financial summary**

	US\$000s	2015	2016	2017	2018e	2019e
Year end 30 June		AASB	AASB	AASB	AASB	AASB
<b>PROFIT &amp; LOSS</b>						
Sales, royalties, milestones		0	0	0	0	7,030
Other (includes R&D tax rebate)		1,244	2,786	6,508	10,031	3,275
Revenue		1,244	2,786	6,508	10,031	10,305
R&D expenses		(4,511)	(7,519)	(8,463)	(8,080)	(10,800)
SG&A expenses		(2,484)	(3,301)	(5,761)	(3,806)	(3,724)
Other		0	0	0	0	0
EBITDA		(5,751)	(8,034)	(7,716)	(1,855)	(4,219)
Operating Profit (before GW and except.)		(5,755)	(8,110)	(7,806)	(2,159)	(4,438)
Intangible Amortization		(433)	(1,003)	(62)	(1,210)	(1,089)
Exceptionals		848	(432)	0	0	0
Operating Profit		(5,340)	(9,546)	(7,868)	(3,369)	(5,527)
Net Interest		(213)	308	(392)	110	27
Pre-Tax Profit (norm)		(6,401)	(8,805)	(8,260)	(3,259)	(5,500)
Pre-Tax Profit (reported)		(5,553)	(9,237)	(8,260)	(3,259)	(5,500)
Tax benefit		0	0	151	0	0
Profit After Tax (norm)		(6,401)	(8,805)	(8,109)	(3,259)	(5,500)
Profit After Tax (reported)		(5,553)	(9,237)	(8,109)	(3,259)	(5,500)
Average Number of Shares Outstanding (m)		23.8	42.7	46.8	49.2	50.2
Average Number of ADRs Outstanding (m)		2.38	4.27	4.68	4.92	5.02
EPS - normalized (c)		(22.76)	(21.61)	(17.33)	(6.62)	(10.96)
EPS - diluted		(22.76)	(21.61)	(17.33)	(6.62)	(10.96)
Dividend per share (c)		0.0	0.0	0.0	0.0	0.0
Earnings per ADR - normalized (c)		(227.6)	(216.1)	(173.3)	(66.2)	(109.6)
Earnings per ADR - diluted (c)		(227.6)	(216.1)	(173.3)	(66.2)	(109.6)
Dividend per ADR (c)		0.0	0.0	0.0	0.0	0.0
<b>BALANCE SHEET</b>						
Fixed Assets		1,133	1,084	12,487	17,908	16,676
Intangible Assets		1,056	625	12,098	10,888	9,799
Tangible Assets		65	450	372	1,094	951
Investments		12	10	17	5,926	5,926
Current Assets		33,933	25,908	14,805	6,414	5,952
Stocks		0	0	0	0	0
Debtors		114	151	3,240	3,128	3,373
Cash		33,722	25,424	10,986	2,706	2,000
Other		96	333	580	580	580
Current Liabilities		(1,351)	(1,088)	(4,092)	(4,092)	(3,020)
Creditors		(1,230)	(988)	(1,423)	(1,423)	(352)
Short term borrowings		0	0	0	0	0
Other		(121)	(100)	(2,669)	(2,669)	(2,669)
Long Term Liabilities		0	(117)	(3,943)	(3,943)	(8,503)
Long term borrowings		0	0	0	0	(4,560)
Other long term liabilities		0	(117)	(3,943)	(3,943)	(3,943)
Net Assets		33,715	25,788	19,257	16,287	11,105
<b>CASH FLOW</b>						
Operating Cash Flow		(4,377)	(9,411)	(8,879)	(7,363)	(5,218)
Net Interest		0	308	189	110	27
Tax		0	0	0	0	0
Capex		(74)	(399)	(15)	(1,026)	(76)
Acquisitions/disposals		6	2	(5,394)	0	0
Equity Financing		36,035	594	(13)	0	0
Dividends		0	0	0	0	0
Other		0	0	0	0	0
Net Cash Flow		31,590	(8,906)	(14,113)	(8,279)	(5,267)
Opening net debt/(cash)		156	(33,722)	(25,424)	(10,986)	(2,706)
HP finance leases initiated		0	0	0	0	0
Other		2,288	608	(326)	0	0
Closing net debt/(cash)		(33,722)	(25,424)	(10,986)	(2,706)	2,560

Source: Kazia Therapeutics accounts, Edison Investment Research. Note: Solely for the convenience of the reader the financial summary table has been converted at a rate of US\$0.76 to A\$1. Kazia Therapeutics reports statutory accounts in Australian dollars. These translations should not be considered representations that any such amounts have been or could be converted into US dollars at the assumed conversion rate.

Contact details	Revenue by geography
Level 24 Three International Towers 300 Barangaroo Ave Sydney, NSW Australia Tel: +61 2 9472 4101 www.kaziatherapeutics.com	N/A
Management team	Chairman: Iain Ross
<b>CEO: Dr James Garner</b> Dr Garner is an experienced life sciences executive who has previously worked with companies ranging from small biotechs to multinational pharmaceutical companies such as Biogen and Takeda. His career has focused on regional and global development of new medicines from preclinical to commercialization. Dr Garner is a physician by training and holds an MBA from the University of Queensland. He began his career in hospital medicine and worked for a number of years as a corporate strategy consultant with Bain & Company before entering the pharmaceutical industry. Prior to joining Kazia in 2016, he led R&D strategy for Sanofi in Asia-Pacific and was based in Singapore.	Iain has held senior positions in Sandoz, Fisons, Hoffmann-La Roche and Celltech Group and also undertaken a number of start-ups and turnarounds on behalf of banks and private equity groups. His track record includes multiple financing transactions having raised in excess of £300m, both publicly and privately, as well as extensive experience of divestments and strategic restructurings. He has over 20 years' experience in cross-border management as a chairman and CEO. He is chairman of e-Therapeutics (LSE:ETX), Redx Pharma (LON:REDX) and Biomer Technology.
Principal shareholders at June 2017	(%)
HSBC Custody Nominees	35.6
Hishenk	5.6
Companies named in this report	
Roche, Noxopharm	

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