BELL POTTER

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Speculative

See key risks on Page 5 and Biotechnology Risk Warning on Page 7. Speculative securities may not be suitable for Retail Clients.

Analyst
John Hester 612 8224 2871

Authorisation
TS Lim 612 8224 2810

Kazia Therapeutics

Paxalisib Joins A Second Platform Study

Recommendation
Buy (unchanged)
Price
$1.33
Valuation
$2.76 (unchanged)
Risk
Speculative

GICS Sector

Pharmaceuticals & Biotechnology

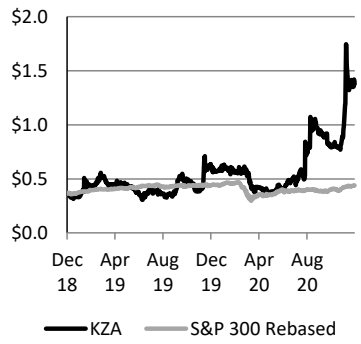
Expected Return	
Capital growth	**107.5%**
Dividend yield	**0.0%**
Total expected return	**107.5%**

Company Data & Ratios	
Enterprise value	**$192.6m**
Market cap	**$167.6m**
Issued capital	**126.2m**
Free float	**99%**
Avg. daily val. (52wk)	**0**
12 month price range	**$0.35 - $1.78**

Price Performance

	(1m)	(3m)	(12m)
Price (A$)	0.82	0.97	0.62
Absolute (%)	67.68	42.06	120.74
Rel market (%)	59.75	29.29	120.81

Absolute Price



SOURCE: IRESS

Paxalisib to participate in a second platform study

KZA has announced its intention to participate in a second platform study, this time to treat the rare paediatric childhood brain cancer known as diffuse midline gliomas including diffuse intrinsic pontine glioma (DIPG). The trial will be completely funded and run by the US based not for profit organisation, the Pacific Paediatric Nero-Oncology Consortium (PNOC). KZA has agreed to supply drug (paxalisib) only to the study and in return will be entitled to unencumbered rights to data. The market size for this indication is small (i.e. ~300 patients per year in the US for DIPG), nevertheless the opportunity cost is modest, while the upside from more data and a potential additional indication could add significantly to the commercial appeal of paxalisib.

There are three drugs involved in the study and several patient cohorts including a treatment naive group and those with recurrent disease. Patients will be treated with one of two drug combinations. The experimental drug ONC201 (in development by the privately held US biotech firm Oncoceutics) will be common to all patients with either paxalisib or another investigational drug - Panobinostat.

The trial is expected to commence enrolment in 1H CY21 in the US and is likely to expand internationally. Patient numbers are not specific at this time as the study is an adaptive design, hence investigators will investigate various avenues and pursue the most promising. The data from this trial may also be used to inform future studies. In the event that one of the drug combinations involving paxalisib shows safety and efficacy the strength of the signal will have a bearing on any approval pathway. Approval of two drugs as a combination therapy is entirely acceptable to the FDA and other regulators. We do not expect the data from PNC022 will impact the current phase III study in GBM (being the GBM Agile study) and subsequent registration process.

Maintain Buy Rating

There are no changes to earnings. We maintain our Speculative Buy rating and valuation of $2.76.

Earnings Forecast

June Year End	FY20	FY21e	FY22e	FY23e
Revenues	1.0	4.3	4.5	46.2
EBIT $m	-12.7	-19.7	-10.5	32.2
NPAT (underlying) $m	-12.4	-19.5	-10.6	32.1
NPAT (reported) $m	-12.4	-19.5	-10.6	32.1
EPS underlying (cps)	-17.0	-15.4	-8.4	25.3
EPS growth %	nm	nm	nm	nm
PER (x)	nm	nm	nm	5.3
FCF yield (%)	nm	nm	nm	nm
EV/EBITDA (x)	nm	nm	nm	nm
Dividend (cps)	-	-	-	-
Franking	0%	0%	0%	100%
Yield %	0%	0%	0%	0%
ROE %	-88%	-97%	-112%	77%

SOURCE: BELL POTTER SECURITIES ESTIMATES

Diffuse Intrinsic Pontine Glioma

Parts of this section are taken from the abstract of published research by Perrone et al.[1]

Diffuse intrinsic pontine glioma (DIPG) mainly affects children with a median age of 6-7 years old. It accounts for 10% of all paediatric tumours. Unfortunately, DIPG has a poor prognosis, and the median survival is generally less than 2 years. The standard of care is radiotherapy with anti tumoural agents – none of which are particularly effective. The two year survival rate is ~10% and the five year survival rate is 2%.

There are about 300 cases of DIPG per year in the United States, hence this is a small market and one which does not attract significant attention from large pharma companies.

The value proposition for KZA from its participation in this study is:

- there almost no opportunity cost i.e. the company is contributing drug only;
- while the market in DIPG is not large, if successful the additional data will help validate the paxalisib mechanism of action in an adjacent indication to glioblastoma. Consistency of clinical impact across more tumour types is highly complimentary;
- if successful the trial may result in more data and an additional approval.

On a risk/reward basis, the potential rewards far outweigh any downside risk.

ONC201

ONC201 is a highly selective antagonist of dopamine receptor D2 (DRD2) and ClpP agonist that is able to penetrate the blood-brain-barrier effectively. ONC201 is currently in a pivotal trial for H3 K27 M-mutant gliomas and is in Phase II trials in a variety of oncology indications, such as neuroendocrine tumors, endometrial cancer, and acute myeloid leukemia.

Although the drug is known to target certain cell receptors, the mechanism of action for its oncolytic effect remains largely unknown.

Based on its lead indication, the FDA granted to ONC201 Fast Track Designation for the treatment of adult recurrent H3 K27 M-mutant high-grade glioma, Orphan Drug Designation for the indication of glioblastoma and H3 K27M-mutant glioma, and Rare Pediatric Disease Designation for treatment of H3 K27 M mutant gliomas.

In the absence of efficacy data from a randomised study in DIPG, the anecdotal evidence supporting its use is encouraging. One ten year old female patient with DIPG was enrolled in an investigator lead compassionate use study. She had initially presented with severe facial palsy and universal hearing loss. She had minimal response to radiotherapy following which ONC201 treatment was initiated.

Tumour volume subsequently decreased by 44% over 6 months and remained stable at 18 months. Neurological symptoms eased with hearing returning and the facial palsy improved from grade 4 to grade 1. After 1 year new tumours emerged (which were again treated with chemotherapy and Avastin) and subsequently remained stable.

There were no serious adverse events associated with ONC201. The patient remains alive and clinically improved 22 months from diagnosis.

H3 K27 M MUTATION

About 10% of adults with glioma have the H3 K27 M mutation. About 50-60% of children with high-grade glioma (and 80-90% of children with Diffuse Intrinsic Pontine Gliomas, or

[1] Perrone et al, 2020 Aug 5. doi: 10.2174/0929867327666200806110206.Online ahead of print.

DIPG) have the H3 K27 M mutation. The test is commercially available and easily accessible either through immunohistochemistry (IHC) staining or gene sequencing.

Panobinostat

Panobinostat (Brand name Farydak) received accelerated approved for the treatment of multiple myeloma in 2015. Patients must have first failed 2 previous treatment lines, hence it is a 3rd line treatment. The drug is being marketed by Novartis and was developed by Securabio (unlisted US biotech). Clinical trials in multiple myloma are ongoing. This appears to be a nasty drug causing severe Diarrhea (grade 3 and 4 in 25% of patients) as well as cardiac toxicity and does not appear suited to paediatric use.

We found no published data in relation to its treatment of DIPG or diffuse midline gliomas. Clinical evidence is likely to have come from anecdotal patient use.

Pacific Paediatric Neuro Oncology Consortium (PNOC)

PNOC was formed to provide children with brain tumours access to innovate treatments. It pursues clinical strategies that are based on the molecular and genetic composition of each tumour. The clinical trials test new therapies aimed at interfering with specific cellular pathways or mutations after confirming the patient's tumour has those characteristics, thereby sparing patients from treatment not suited to their tumour type. The group has conducted numerous clinical trials, many of which have not been successful, hence the group is not afraid to fail fast and move on.

The core values of the group are: to drive innovation; to collaborate and finally to be bold.

PNOC appears to be privately funded as had study sites in Australia, Canada, United States and several countries in Europe.

The clinical trial in which Paxalisib will be involved is fully funded by PNOC. The trial design is not specified in great detail however, we do know the following:

- All patients will first receive ONC201 with either Paxalisib or Panobinostat;
- It is reasonable to assume that all patients will be first screened for the H3 K27 M mutation and only those positive for that mutation will be admitted to the trial;
- The study will include separate cohorts comprising differing patient groups including
    - newly diagnosed disease;
    - patients who have completed initial radiotherapy; and
    - patients who have experienced disease progression after treatment.
- Primary endpoints will be proportion of patients with progression free survival at 6 months for newly diagnosed patients and overall survival for recurrent patients.

Professor Matthew Dun – University of Newcastle is a scientific adviser to the study. We understand Professor Dun has conducted extensive research work in this indication with Paxalisib and ONC201.

Patient numbers are not specified. Investigators are likely to conduct multiple experiments and pursue the most promising. It is likely dozens of patients will be involved.

PROSPECTIVE REGULATORY APPROVAL

The trial itself is conducted under and investigator sponsored IND. The IND attaches to the lead investigator – in this case Professor Sabine Mueller at U. California.

Each of the parties in these studies has unencumbered access to the data from the study. In the event that a combination involving paxalisib does show promising efficacy, the

registration pathway would be determined by the strength of the signal and safety profile. Neither Paxalisib or ONC201 are approved in any indication at this time.

Paxalisib is a new chemical entity but designed to treat the PI3K pathway. ONC201 is a novel drug and mechanism of action remains largely unknown. In our view it is likely the FDA would require a small randomised trial for approval. There is no requirement for the two drugs to be combined into a single molecule i.e. the combination is approvable.

Approval as a combination is also likely to bring a raft of new opportunities for additional patent protection measures.

In the event of a successful combination study there are many questions to be resolved regarding commercialisation. Despite this, the indication is small – perhaps 2,000 patients in DIPG globally each year. While the price for the drug combination may be significant (i.e. >US$100K per year of treatment in the US) the overall dollar value of the market is modest.

Commencement of the study remains subject to execution of a definitive contract and is dependent on approval by the US FDA and Institutional Review Boards. It is expected that PNOC022 will initially open in the United States in 1H CY 2021, with expansion to other countries including Australia taking place in CY2021.

Figure 1 - Clinical Trial Program Overview

	Indication	Stage	n	Progress	Design	Sponsor	Registration
Paxalisib	Glioblastoma	Phase II	30	Completed recruitment	Single Arm, open label	Kazia Thereapeutics	NCT03522298
	Glioblastoma	Phase II/III	up to 200	Ethics approvals	Three treatment cohorts. Randomised controlled study	Alliance for clinical trials in Oncology and Genentech	NCT03970447
	DIPG (childhood brain cancer)	Phase II	27	Active, Not Recruiting	Various treatment cohorts on paxalisib and radiation therapy	St Jude Children's Research Hospital	NCT03696355
	Primary CNS Lymphoma	Phase II	25	Ethics approvals	Single Arm, open label	Dana Farber Cancer Institute	Not yet registered
	Brain Metastases	Phase II	150	Recruiting	Any brain metastses with clinically validated alternation in PI3K pathway	National Cancer Institute	NCT03994796
	Brain metastases - breast cancer	Phase II	47	Recruiting	Non randomised, single arm, combination study of Paxalisib with Trastuzumab	Dana Farber Cancer Institute	NCT03765983
	Brain Metastases - any source	Phase 1	36	Recruiting	3+3 dose escalation cohorts on paxalisib and radiation therapy	Memorial Sloan Kettering	NCT04192981
	Diffuse midline gliomas including DIPG	Unspecified	TBA	Ethics approval	Multiple arm study including three drugs one of which is paxalisib. Patients are either niave or recurring	Pacific Paediatric Neuro -oncology consortium	TBA
Cantrixil	Recurrent Ovarian Cancer	Phase 1	28	Reported Results	Part A - dose escalation, Part B Expansion Cohort	Kazia Thereapeutics	NCT02903771

SOURCE: COMPANY DATA

Paxalisib belongs to a drug class (PI3K) where there are already multiple drugs on market (though none indicated for glioblastoma) and where the mechanism of action is well understood. Generally new cancer therapies are approved on the basis of a single phase III, particularly in disease with Orphan indication.

CANTRIXIL

Earlier this month the KZA reported top line data from its phase 1 study of Cantrixil in ovarian cancer.

Overall, 16 patients were evaluable for efficacy. One patient demonstrated a complete response and two patients experienced a partial response for making an overall response rate (ORR) of 19%.

These are promising results in this heavily pre-treated group of patients. The company is likely to seek a development partner for the drug as the next step in its development.

KZA management will remain focussed on the development of paxalisib as a priority.

Risk Areas

The key risk include but are not limited to the follow items:

Kazia's ability to achieve profitability is dependent on a number of factors, including its ability to complete successful clinical trials, obtain regulatory approval for its products and successfully commercialise or partner both Paxalisib and Cantrixil. There is no guarantee that the company will achieve these goals.

Kazia does not currently generate revenue from product sales and revenues are not anticipated in the short to medium term. The company is likely to continue to rely on shareholders to fund the business of the foreseeable future.

Clinical trial risk

KZA may be unable to secure necessary approvals from regulatory agencies and institutional bodies (clinics and hospitals) to conduct future clinical trials. There is also no assurance that either of the drugs under development will prove to be safe and efficacious in clinical trials, or that the regulatory approval to manufacture and market its products will be received. Clinical trials might also potentially expose the Company to product liability claims in the event its products in development have unexpected effects on clinical subjects.

Paxalisib and Cantrixil must both undergo a comprehensive and highly regulated development and review process before receiving approval for marketing.

The company is also dependent on commercially attractive markets remaining available to it during the commercialisation phase and there is a risk that, once developed and ready for sale, commercial sales to fund sufficient revenues for continued operations and growth, may not be achieved.

Arrangements with third-party collaborators

Kazia may pursue collaborative arrangements with pharmaceutical and life science companies, academic institutions or other partners to complete the development and commercialisation of its products (including for the GBM Agile study). These collaborators may be asked to assist with funding or performing clinical trials, manufacturing, regulatory approvals or product marketing. There is no assurance that Kazia will attract and retain appropriate strategic partners or that any such collaborators will perform and meet commercialisation goals. If Kazia is unable to find a partner, it would be required to develop and commercialise its products at its own expense. This may place significant demands on the Company's internal resources and potentially delay the commercialisation.

Requirement to raise additional funds

The company may be required to raise additional equity or debt capital in the future. There is no assurance that it will be able to raise that capital when it is required or, even if available, the terms may be unsatisfactory. If the company is unsuccessful in obtaining funds when they are required, it may need to delay or scale down its operations.

Intellectual property

The company's ability to leverage its innovation and expertise depends upon its ability to protect its intellectual property and any improvements to it. The intellectual property may not be capable of being legally protected, it may be the subject of unauthorised disclosure or be unlawfully infringed, or the company may incur substantial costs in asserting or defending its intellectual property rights.

Kazia Therapeutics
as at 14 December 2020

Recommendation	Buy, Speculative
Valuation	$1.33
Target (12 months)	$2.76

Table 1 - Financial summary

`	FY19	FY20	FY21e	FY22e	FY23e
Year Ending June					
R&D incentive	1.4	1.0	4.3	4.5	4.5
Total Revenue	**1.5**	**1.0**	**4.3**	**4.5**	**46.2**
COGS	-	-	-	-	-
Gross profit	1.5	1.0	4.3	4.5	46.2
Expenses Net of R&D	-6.5	-9.5	-19.0	-10.0	-8.0
Other expenses	-3.9	-3.2	-5.0	-5.0	-6.0
Total Expenses	-12.2	-13.7	-24.0	-15.0	-14.0
EBIT	-10.7	-12.7	-19.7	-10.5	32.2
Interest income	0.0	0.0	0.2	-0.1	-0.1
Pre tax profit	(10.6)	(12.7)	(19.5)	(10.6)	32.1
Tax expense	0.3	0.3	-	-	-
NPAT- normalised	**(10.3)**	**(12.4)**	**(19.5)**	**(10.6)**	**32.1**
Reported NPAT	(10.3)	(12.4)	(19.5)	(10.6)	32.1

Cashflow (A$m)	FY19	FY20	FY21e	FY22e	FY23e
Gross cashflow	-6.7	-8.8	-19.6	-10.4	32.3
Net interest	0.0	0.0	0.2	-0.1	-0.1
Operating cash flow	-6.7	-8.8	-19.4	-10.5	32.2
Proceeds from asset sales	2.4	0.0	0.0	0.0	0.0
Free cash flow	-4.3	-8.8	-19.4	-10.5	32.2
Business acquistions	0.0	0.0	0.0	0.0	0.0
Proceeds from issuance	3.8	12.1	25.6	0.0	0.0
Movement in borrowings	0.0	0.0	0.0	0.0	0.0
Other	0.0	0.0	0.0	0.0	0.0
Change in cash held	-0.5	3.3	6.2	-10.5	32.2
Cash at beginning of period	6.0	5.4	8.7	14.9	4.4
FX adjustment	-0.1	0.0	0.0	0.0	0.0
Cash at year end	**5.4**	**8.7**	**14.9**	**4.4**	**36.5**

Balance Sheet (A$m)	FY19	FY20	FY21e	FY22e	FY23e
Cash	5.4	8.7	14.9	4.4	36.5
Receivables	1.7	1.4	1.4	1.4	1.4
Other current assets	0.4	0.5	0.5	0.5	0.5
Property, Plant and Equipment	-	-	-	-	-
Intangibles	13.5	12.4	12.4	12.4	12.4
Other non current assets	0.2	-	-	-	-
Total assets	21.2	23.0	29.1	18.6	50.8
Trade payables	1.8	3.5	3.5	3.5	3.5
Other liabilities	1.4	1.8	1.9	2.0	2.1
Deferred taxes	3.7	3.4	3.4	3.4	3.4
Provisions	0.1	0.2	0.2	0.2	0.2
Total Liabilities	7.0	8.9	9.0	9.1	9.2
Net Assets	14.2	14.1	20.1	9.5	41.6
Share capital	36.6	48.8	74.4	74.4	74.4
Other equity	2.5	1.5	1.4	1.4	1.4
Retained earnings	(24.9)	(36.2)	(55.7)	(66.3)	(34.2)
Reserves	-	-	-	-	-
Shareholders Equity	14.2	14.1	20.1	9.5	41.6

Valuation Ratios (A$m)	FY19	FY20	FY21e	FY22e	FY23e
Reported EPS (cps)	-16.6	-17.0	-15.4	-8.4	25.3
Normalised EPS (cps)	-16.6	-17.0	-15.4	-8.4	25.3
EPS growth (%)	nm	nm	nm	nm	nm
PE(x)	**nm**	**nm**	**nm**	**nm**	**5.3**
EV/EBIT (x)	nm	nm	nm	nm	nm
P/NTA (x)	118.0	74.0	21.9	- 58.1	-
Book Value Per Share (cps)	22.9	14.9	15.9	7.5	32.9
Price/Book (x)	5.8	8.9	8.4	17.7	4.0
DPS (cps)	-	-	-	-	-
Payout ratio %	0%	0%	0%	0%	0%
Dividend Yield %	0.0%	0.0%	0.0%	0.0%	0.0%
Franking %	0%	0%	0%	0%	0%
FCF yield %	nm	nm	nm	nm	nm
Net debt/Equity	0%	0%	0%	0%	0%
Net debt/Assets	0%	0%	0%	0%	0%
Gearing	net cash	net cash	net cash	net cash	net cash
Net debt/EBITDA (x)	n/a	n/a	n/a	n/a	n/a
Interest cover (x)	n/a	n/a	n/a	n/a	n/a

Interim Results	1H20	2H20	1H21e	2H21e
Revenues	0.6	0.4	0.6	3.7
R&D Expense	-4.2	-5.3	-12.0	-7.0
All Other expenses	-2.4	-0.8	-3.0	-2.0
EBIT	-6.2	-6.5	-7.4	-12.3

SOURCE: BELL POTTER SECURITIES ESTIMATES

Recommendation structure

Buy: Expect >15% total return on a 12 month view. For stocks regarded as 'Speculative' a return of >30% is expected.

Hold: Expect total return between -5% and 15% on a 12 month view

Sell: Expect <-5% total return on a 12 month view

Speculative Investments are either start-up enterprises with nil or only prospective operations or recently commenced operations with only forecast cash flows, or companies that have commenced operations or have been in operation for some time but have only forecast cash flows and/or a stressed balance sheet.

Such investments may carry an exceptionally high level of capital risk and volatility of returns.

Research Team

Staff Member	Title/Sector	Phone	@bellpotter.com.au
TS Lim	Joint Head of Research/Banks	612 8224 2810	tslim
Chris Savage	Joint Head of Research/Industrials	612 8224 2835	csavage
Analysts			
Lafitani Sotiriou	Diversified Financials/Fintech	613 9235 1668	lsotiriou
John Hester	Healthcare	612 8224 2871	jhester
Tanushree Jain	Healthcare	612 8224 2849	tnjain
Elyse Shapiro	Healthcare	613 9235 1877	eshapiro
Steven Anastasiou	Industrials	613 9235 1952	sanastasiou
James Filius	Industrials	613 9235 1612	jfilius
Sam Haddad	Industrials	612 8224 2819	shaddad
Alex McLean	Industrials	612 8224 2886	amclean
Hamish Murray	Industrials	613 9235 1813	hmurray
Jonathan Snape	Industrials	613 9235 1601	jsnape
Damien Williamson	Industrials	613 9235 1958	dwilliamson
Peter Arden	Resources	613 9235 1833	parden
David Coates	Resources	612 8224 2887	dcoates
Stuart Howe	Resources	613 9235 1856	showe
Associate			
Joseph House	Associate Analyst	+61 3 9235 1624	jhouse

Bell Potter Securities Limited
ACN 25 006 390 7721
Level 29, 101 Collins Street
Melbourne, Victoria, 3000
Telephone +61 3 9256 8700
www.bellpotter.com.au

Bell Potter Securities (HK) Limited
Room 1701, 17/F
Posperity Tower, 39 Queens Road
Central, Hong Kong, 0000
Telephone +852 3750 8400

Bell Potter Securities (US) LLC
Floor 39
444 Madison Avenue, New York
NY 10022, U.S.A
Telephone +1 917 819 1410

Bell Potter Securities (UK) Limited
16 Berkeley Street
London, England
W1J 8DZ, United Kingdom
Telephone +44 7734 2929