EDISON

Kazia Therapeutics

Financial update

All in on GBM AGILE, but eyes on brain mets

Pharma & biotech

Patients have officially begun to receive doses of paxalisib as part of the pivotal GBM AGILE study that Kazia is participating in. The Phase II/III study is active in at least 31 sites in the US and Canada currently and is expanding to Europe and China in H121. Given the study design, it is unlikely to report clinical data in 2021, so the near-term focus will be on clinical results from ongoing investigator-sponsored studies, particularly in brain metastases (from other cancer types), which we see as a major potential indication for the drug.

Year end	Revenue (A$m)	PBT* (A$m)	EPS* (A$)	DPS (A$)	P/E (x)	Yield (%)
06/19	1.6	(7.4)	(0.13)	0.00	N/A	N/A
06/20	1.1	(10.8)	(0.14)	0.00	N/A	N/A
06/21e	7.0	(5.8)	(0.05)	0.00	N/A	N/A
06/22e	1.2	(12.3)	(0.09)	0.00	N/A	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

Big readouts coming for brain metastases

We consider brain metastases (BMs) one of the most interesting indications that paxalisib could potentially be used for, and the drug is currently being investigated for this indication in three clinical studies for BMs: one Phase I and two Phase IIs, sponsored by Sloan-Kettering, the NIH and Dana-Farber respectively, all of which are expected to provide data in CY21. In particular we are interested in the product for the treatment of breast cancer brain metastases (BCBMs), which are a major cause of mortality for metastatic breast cancer patients.

Cantrixil finds a new home at Oasmia

Kazia announced on 1 March 2021 that it has licensed its asset cantrixil to Oasmia for further development; Oasmia intends to initiate Phase II studies on the compound starting in 2022. The deal had a US$4m upfront payment, US$42m in milestone payments and double-digit royalties on sales. Cantrixil is a broad-spectrum anti-cancer agent that recently completed Phase I studies in 2020, showing a 19% overall response rate in patients with metastatic ovarian cancer. We are happy to see this partnership because it will ensure the continued development of the program.

Valuation: Increased to A$265.33m or A$2.10

We have increased our valuation to A$265.33m or A$2.10 per basic share, from A$244.1m or A$1.93 per basic share. We have rolled forward our NPVs and added cantrixil back to our models (A$8.47m valuation). We have also updated for the new net cash after the transaction (A$24.97 pro forma). Otherwise, our models remain unchanged. We expect the company to need A$20m in additional capital to reach profitability, and we expect the company to seek one or more partners to address this cash need.

1 March 2021

Price	**A$1.33**
Market cap	**A$167m**
	A$1.40/US$
Net cash (A$m) at 31 December 2020	19.4
Shares in issue	126.2m
Free float	57.3%
Code	KZA
Primary exchange	ASX
Secondary exchange	Nasdaq

Share price performance

%	1m	3m	12m
Abs	(0.7)	0.4	142.6
Rel (local)	1.7	(0.9)	137.3
52-week high/low	A$1.75		A$0.35

Business description

Kazia Therapeutics is a pharmaceutical company with lead asset paxalisib, a PI3K inhibitor licensed from Genentech that can cross the blood-brain barrier, which is entering a pivotal study for GBM. It is also being investigated for other brain cancers such as breast cancer brain metastases.

Next events

Dana-Farber BCBM Phase II	CY21
Sloan-Kettering BM Phase II	CY21
NIH BM Phase II	CY21

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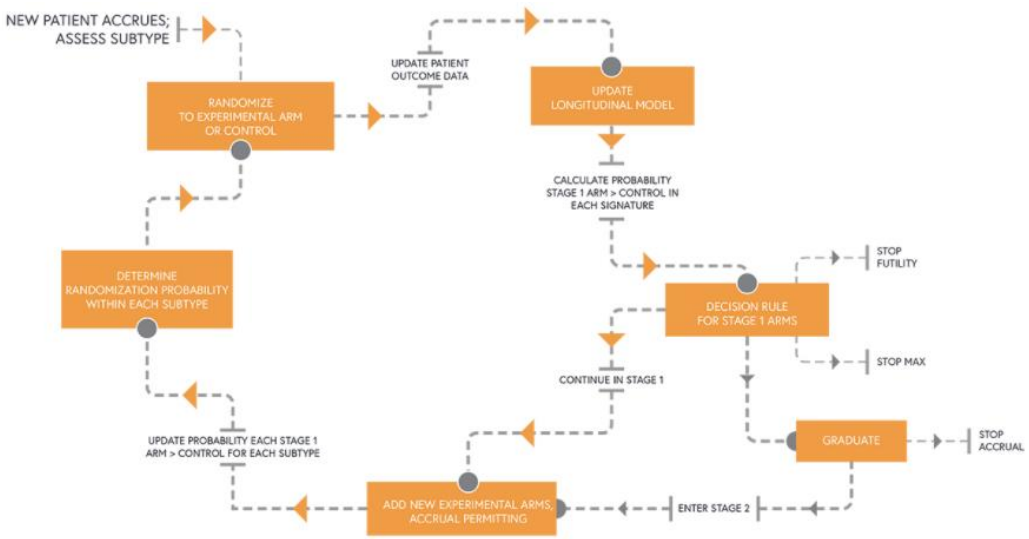
GBM AGILE moving along but the wait begins

Kazia officially announced on 7 January 2021 that the first patients had been enrolled into the paxalisib arm of the GBM agile study. The paxalisib arm of the study is expected to enrol a maximum of 200 patients, although it may be less due to the adaptive design of the trial (Exhibit 1).

The study is composed of two stages, which will run sequentially, with seamless transition from Stage 1 to Stage 2. Stage 1 is a Phase II 'screening stage', which will evaluate paxalisib within newly diagnosed unmethylated and recurrent patient populations, compared against a common control. Stage 1 will stop recruiting patients if it reaches its maximal sample size, shows signs of futility or shows inadequate safety. If paxalisib reaches an efficacy threshold for graduation from Stage 1 to Stage 2 (Phase III), it will seamlessly move into that stage within either or both participating patient groups (newly diagnosed unmethylated and recurrent). Stage 2 is the Phase III 'confirmation stage', with fixed randomization. The primary analysis of paxalisib's efficacy uses all patients in both stages and all control patients in the trial.

The Phase II portion of the study has a higher target enrolment (150 patients) compared to the confirmatory Phase III portion (50 patients), although both of these values represent the upper end of estimates for how many patients will be needed. These patients will be compared against a common control (shared with other active drug arms in the study, which also include Bayer's regorafenib and Kintara Therapeutics' VAL-083) for an estimated total study population of 400 spread across the Phase II and Phase III portions of the study. When the program transitions from a Phase II study (Stage 1) to a Phase III study (Stage 2) is a function of locked data that is independently evaluated. This allows for the program to have this transition as soon as the statistical criteria are met, but prevents the data from being publicly released. We are assuming that at this point that there will be no announcement of the transition out of an abundance of caution.

Exhibit 1: GBM AGILE adaptive design



Source: Global Coalition for Adaptive Research

Most of the other tasks necessary to prepare the drug for approval (assuming positive Phase III data) have already been completed. Management has communicated to us that manufacturing and controls are in place. Paxalisib received a Fast-track Designation in August 2020, which entitles it to undergo a rolling NDA process in which portions of the application package can be submitted piecemeal to expedite the process and provide increased feedback. If the company decides to go down this route, this process may be initiated soon.

Brain met readouts might determine the drug's future

Although we do not expect major news from the GBM AGILE study in the near term, there are multiple other ongoing clinical studies utilising paxalisib that are providing readouts very soon and could potentially shape the direction of this program. In particular, we are interested in the upcoming readouts for three clinical studies investigating the product for the treatment of BMs. BMs are a major cause of mortality in metastatic cancer patients because the blood brain barrier limits the effectiveness of many treatments that work at other metastasis sites. Therefore, paxalisib is well positioned to provide a benefit to these patients as a targeted cancer treatment designed to cross the blood brain barrier. In addition to these BM studies, there are also investigator-sponsored studies for primary central nervous system lymphoma (PCNSL) and diffuse intrinsic pontine glioma (DIPG) that are expected to begin recruiting patients shortly in Q1 CY21

All three ongoing investigator-sponsored studies of BMs are expected to provide readouts in the very near term. The company is hoping to have results in H1 CY21 for each study, but this is subject to the internal timelines of the independent investigators, which is subject to change.

The earliest stage program is a Phase I study at Memorial Sloan-Kettering investigating paxalisib in combination with radiotherapy for any primary tumour type as long as it has PI3K pathway mutations. This study has targeted enrolment of 36, and we expect the main readout to be on the safety of the combination treatment. Another program in Phase II sponsored by the NIH is also investigating BMs from any primary solid tumour. This program is also investigating the CDK4/6 inhibitor Verzenio (abemaciclib, Eli Lilly) and the TRK inhibitor Vitrakvi (entrectinib).

Finally, we are expecting an imminent readout from the Phase II BCBM study being performed at Dana-Farber any day. The company is currently guiding toward the program providing data in H121 (albeit with the above caveats regarding investigator timelines), but previous guidance was for Q420, so the readout is overdue, in our view. This study is investigating the drug in combination with Herceptin (trastuzumab) in HER2+ breast cancer patients. We expect results of this study to be potentially the most informative of the three investigator-sponsored BM programs because we consider the BCBM market the clearest future potential indication for the product outside of primary brain tumours. One retrospective study of patients in Belgium found that among HER2+ breast cancer patients, 10.8% had BMs at their initial screening and 41.7% developed BMs within their lifetime.[1] Survival of these patients was significantly reduced, from 46.7 months for those with no central nervous system involvement to 20.8 months for those with BMs.

Cantrixil finds a new home at Oasmia

Kazia announced on 1 March 2021 that it has licensed cantrixil to Oasmia for a US$4m upfront payment, US$42m in milestone payments and double-digit royalties on sales. We are very pleased with this development because cantrixil was unlikely to be developed internally at Kazia any time soon given the current focus on paxalisib. With this partnership in place, the drug will likely see continued clinical development, and Kazia has the potential of realising some of that value. We previously removed cantrixil from our valuation models pending such a partnership, and with a deal in place, we are adding it back.

We previously reported on the final data from the Phase I study of cantrixil in metastatic ovarian cancer, in which the drug demonstrated a 19% overall response rate. The company stated in the press release for the deal with Oasmia that it intends to publish the complete data from the Phase I study in CY21. Oasmia is targeting re-entering the clinic with the drug in 2022.

[1] Maurer C, et al. (2018) Risk factors for the development of brain metastases in patients with HER2-positive breast cancer. *ESMO Open* 3, e000440.

Valuation

We have increased our valuation to A$265.33m or A$2.10 per basic share, from A$244.1m or A$1.93 per basic share. The increase is driven by rolling forward our NPVs, and by the re-addition of cantrixil to our models. We assume that the product will be marketed for ovarian cancer and receive its first approval in 2027, similar to our previous assumptions. These may change if Oasmia intends to market the drug for a particular subset of this indication. We assume the milestones will be split between clinical and regulatory milestones (US$12m) and sales milestones (US$30m), and that Kazia will receive a 12% royalty on sales. We include the upfront payment in our new net cash calculation (A$25.0m pro forma after including the Oasmia upfront payment, up from A$23.2m previously). We are conservative regarding our outlook for the drug's approval (15% probability of success) based on the previously reported clinical data. We may update this when the complete data from the Phase I study is published in a scientific journal in 2021.

Exhibit 2: Valuation of Kazia

Development program	Indication	Clinical stage	Prob. of success	Launch year	Patent/ exclusivity protection	Launch pricing (US$/course)	Peak sales (US$m)	rNPV (A$m)
Paxalisib	GBM	Phase II	35%	2025	2037	169,000	450	223.28
	BCBMs	Phase II	5%	2029	2037	183,000	249	8.61
Cantrixil	OC	Phase I complete	15%	2027	2040	124,000	174	8.47
Total								240.36
Net cash and equivalents (fiscal Q221 + Oasmia upfront) (A$m)								24.97
Total firm value (A$m)								265.33
Total basic shares (m)								126.2
Value per basic share (A$)								2.10
Dilutive options (m)								4.54
Total diluted shares								130.70
Value per diluted share								2.06

Source: Kazia Therapeutics reports, Edison Investment Research

Financials

Kazia reported the results for its fiscal half-year ending December 2020 on 24 February 2021 and reported an operating loss of A$6.5m. This was close to our estimates (c A$6.4m), but we have now rebalanced some of our costs between R&D and SG&A in our forecasts for FY22. This has slightly reduced the expected R&D rebate for FY22 (A$1.2m from A$1.5m). During H1 of FY21 the company delivered a deposit of A$7.0m for the GBM AGILE study, which drove much of the higher than average operational cash burn (A$12.3m vs A$2.7m in fiscal H120) during the period. This payment is amortised in our models over the fiscal years FY21–24. Additionally, we have added the upfront payment from Oasmia as revenue in FY21.

The company successfully raised A$23.6m net during the period from a rights offering (31.5m shares at A$0.80), which brings its cash at the end of the period to A$19.4m. We continue to expect the company to need A$20m in additional capital to finance the clinical development of paxalisib. We account for this financing as illustrative debt in FY23, but we expect the company to attempt to address it primarily through licensing activity. The company has stated that it expects 'the commercialisation of paxalisib to occur in the context of a partnership with one or more larger companies.' Now is an opportune time for these discussions to occur so we expect an increased focus on partnering from management.

Exhibit 3: Financial summary

$'k	2019	2020	2021e	2022e
Year end 30 June	IFRS	IFRS	IFRS	IFRS
INCOME STATEMENT				
Revenue	1,565.0	1,060.9	7,004.8	1,211.1
Cost of Sales	0.0	0.0	0.0	0.0
Gross Profit	1,565.0	1,060.9	7,004.8	1,211.1
R&D	6,475.6	9,494.3	8,185.0	6,645.0
SG&A	3,785.6	3,689.9	5,999.9	8,219.9
EBITDA	(7,365.3)	(10,776.8)	(5,833.6)	(12,307.4)
Normalised operating profit	(7,365.4)	(10,776.8)	(5,833.6)	(12,307.4)
Amortisation of acquired intangibles	(1,084.3)	(1,084.3)	(1,084.3)	(1,084.3)
Exceptionals	(1,872.3)	(642.4)	0.0	0.0
Share-based payments	(246.4)	(262.1)	(262.1)	(262.1)
Reported operating profit	(10,568.5)	(12,765.7)	(7,180.1)	(13,653.8)
Net Interest	0.0	0.0	0.0	0.0
Joint ventures & associates (post tax)	0.0	0.0	0.0	0.0
Exceptionals	0.0	0.0	0.0	0.0
Profit Before Tax (norm)	(7,365.4)	(10,776.8)	(5,833.6)	(12,307.4)
Profit Before Tax (reported)	(10,568.5)	(12,765.7)	(7,180.1)	(13,653.8)
Reported tax	298.2	298.2	274.0	521.1
Profit After Tax (norm)	(7,365.4)	(10,365.5)	(5,611.0)	(11,837.7)
Profit After Tax (reported)	(10,270.3)	(12,467.5)	(6,906.1)	(13,132.7)
Minority interests	0.0	0.0	0.0	0.0
Discontinued operations	0.0	0.0	0.0	0.0
Net income (normalised)	(7,365.4)	(10,365.5)	(5,611.0)	(11,837.7)
Net income (reported)	(10,270.3)	(12,467.5)	(6,906.1)	(13,132.7)
Basic average number of shares outstanding (m)	58	73	118	133
EPS - basic normalised (A$)	(0.13)	(0.14)	(0.05)	(0.09)
EPS - diluted normalised (A$)	(0.13)	(0.14)	(0.05)	(0.09)
EPS - basic reported (A$)	(0.18)	(0.17)	(0.06)	(0.10)
Dividend (A$)	0.00	0.00	0.00	0.00
BALANCE SHEET				
Fixed Assets	13,662.3	12,410.1	17,496.4	14,412.0
Intangible Assets	13,494.5	12,410.1	11,325.8	10,241.5
Tangible Assets	0.0	0.0	0.0	0.0
Investments & other	167.8	0.0	6,170.6	4,170.6
Current Assets	7,514.2	10,653.6	22,182.1	12,042.4
Stocks	0.0	0.0	0.0	0.0
Debtors	1,710.7	1,352.3	1,531.5	796.3
Cash & cash equivalents	5,433.9	8,764.0	20,113.3	10,708.7
Other	369.6	537.3	537.3	537.3
Current Liabilities	(1,900.3)	(5,067.5)	(3,494.2)	(3,661.9)
Creditors	(1,763.9)	(3,488.9)	(3,165.6)	(3,333.3)
Tax and social security	0.0	0.0	0.0	0.0
Short term borrowings	0.0	0.0	0.0	0.0
Other	(136.4)	(1,578.5)	(328.5)	(328.5)
Long Term Liabilities	(5,081.4)	(3,870.7)	(5,093.3)	(4,572.2)
Long term borrowings	0.0	0.0	0.0	0.0
Other long-term liabilities	(5,081.4)	(3,870.7)	(5,093.3)	(4,572.2)
Net Assets	14,194.8	14,125.6	31,090.9	18,220.3
Minority interests	0.0	0.0	0.0	0.0
Shareholders' equity	14,194.8	14,125.6	31,090.9	18,220.3
CASH FLOW				
Op Cash Flow before WC and tax	(7,365.3)	(10,776.8)	(5,833.6)	(12,307.4)
Working capital	352.9	1,669.1	(6,700.5)	2,381.7
Exceptional & other	298.2	298.2	274.0	521.1
Tax	0.0	0.0	0.0	0.0
Net operating cash flow	(6,714.2)	(8,809.5)	(12,260.1)	(9,404.5)
Capex	0.0	0.0	0.0	0.0
Acquisitions/disposals	0.0	0.0	0.0	0.0
Net interest	0.0	0.0	0.0	0.0
Equity financing	3,815.7	12,139.7	23,609.3	0.0
Dividends	0.0	0.0	0.0	0.0
Other	2,359.1	0.0	0.0	0.0
Net Cash Flow	(539.4)	3,330.2	11,349.2	(9,404.5)
Opening net debt/(cash)	(5,956.2)	(5,433.9)	(8,764.0)	(20,113.3)
FX	17.1	0.0	0.0	0.0
Other non-cash movements	0.0	0.0	0.0	0.0
Closing net debt/(cash)	(5,433.9)	(8,764.0)	(20,113.3)	(10,708.7)

Source: Kazia Therapeutics reports, Edison Investment Research

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