Biotechnology

KZIA - NASDAQ October 14, 2021

Closing Price 10/13/21	**$10.71**
Rating:	Buy
12-Month Target Price:	$18.00
52-Week Range:	$5.55 - $15.85
Market Cap (M):	141.4
Shares O/S (M):	13.2
Float:	98.0%
Avg. Daily Volume (000):	24.8
Debt (M):	$0.0
Dividend:	$0.00
Dividend Yield:	0.0%
Risk Profile:	Speculative
Fiscal Year End:	June

Total Expenses ('000)

	2021A	2022E	2023E
H1	AUD6,545	AUD11,903	AUD13,688
H2	AUD17,589	AUD12,895	AUD14,829
FY	AUD24,133	AUD24,798	AUD28,517

Kazia Therapeutics is listed on the ASX (KZA) and with ADR's traded on NASDAQ (KZIA). 1 ADR = 10 ordinary Kazia shares. Modeling and historical financials are recorded in AUD while the price target, current price, and market data are translated into USD.

EVENT INFORMATION

Society for Neuro-Oncology (SNO)

November 18-21

Boston, MA

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Kazia Therapeutics Limited

Buy

Taming PI3K Activation to Treat Brain Cancers – Initiating Coverage with a Buy and $18 PT

Summary

- **Kazia is developing two novel, oncology drug candidates: paxalisib (for brain cancers) and EVT801 (for solid tumors).**
- **A validated target. Kazia's lead drug candidate, paxalisib, is a small molecule inhibitor of the PI3K- AKT- mTOR pathway. Since the accelerated approval of TG Therapeutics' (TGTX - NR) umbralisib on February 5, there are now 5 approved PI3K inhibitors on the market.**
- **…but paxalisib could be 'best-in-breed' with a differentiated PI3K profile. While most PI3K inhibitors cannot cross the blood-brain barrier and have been plagued with safety issues, paxalisib's safety profile has been modest to date.**
- **Paxalisib is in 9 clinical trials. Kazia is advancing paxalisib in 1L glioblastoma multiforme (GBM) patients. Having garnered considerable traction among clinicians at prominent academic institutions, paxalisib is currently in 9 trials for CNS-based cancers, including the groundbreaking pivotal GBM AGILE study. We think continued positive readout in GBM could read positive to other CNS indications such as brain metastases.**
- **Conclusion. GBM represents a challenging indication and the current stock price reflects the risks around GBM. but not the upside potential, in our view. We model peak ~$275M global market opportunity (partially partnered) in GBM. Several readouts (interim/final) for paxalisib are expected before year-end. We believe more positive data from the ongoing studies in 2021/2022 should further de-risk the drug's safety/efficacy profile and, accordingly support a higher valuation.**

Details

Paxalisib – path to registration via GBM AGILE. Established by the collective work of over 130 leading experts in GBM from more than 40 leading institutions, the GBM AGILEtrial is tailored to streamline the discovery of treatments. Importantly for Kazia, the trial is intended to serve as the pivotal study for paxalisib in multiple markets, including the US, EU, and China. How does it work? Traditional P2 and P3 studies have two arms with preset patient populations and sample sizes to address a single question. GBM AGILE is a departure from this and is driven by a nonprofit, international partnership known as GCAR (Global Coalition for Adaptive Research). Of importance, GCAR is also supported by the FDA and other regulatory agencies. The physician-led GBM AGILE trial itself is a two-stage, multi-arm, platform, adaptive Phase 2/3 trial that is being conducted under one master protocol. It allows for multiple therapies or combinations of therapies from different biotech/pharma partners to be evaluated in concert. The study is designed to investigate the therapies in both newly diagnosed and recurrent GBM patient populations (in biomarker-defined populations) vs. one rolling control group (soc) for those therapies. The primary endpoint is overall survival; secondary endpoints include progression free survival and tumor response. Kazia's paxalisib joined the International GBM AGILE study in Oct. 2020. Bayer's (BAYRY - NR) regorafenib was the first drug to be included into the trial, followed by pax. This was followed by Kintara's (KTRA - Buy) VAL-083. Most importantly for Kazia, GBM AGILE provides pax an expedited path to registration, offering an existing infrastructure that allows for faster recruitment while reducing costs. We expect results from the study for the paxalisib arm around mid-CY23, with potential for regulatory approval in CY24.

Compelling valuation. We model the launch of paxalisib in GBM in the US, EU, and China in 2024; and in brain metastases in the US in 2025 and in the EU and China in 2026, with a 70% risk adjustment. A 30% discount is applied to the free cash flow, discounted EPS, and sum-of-the-parts models, which are equally weighted to derive a 12-month price target of $18 USD.

CORPORATE PROFILE

Kazia Therapeutics Limited
Three International Towers
Level 24, 300 Barangaroo Avenue
Sydney NSW, Australia
www.kaziatherapeutics.com

Investment Risk: Kazia's products are not approved, and the company currently does not generate revenue from its product candidates. As a clinical-stage company, Kazia may not turn profitable in the near future.

Regulatory Risk: Kazia's products may fail to demonstrate efficacy and thus may fail to demonstrate meaningful clinical benefit in trials, and/or may have unexpected safety issues, and may not meet the requirements for regulatory approval(s).

Commercial Risk: If/when Kazia's products become commercially available they may not achieve significant market share. In addition, the company lacks commercial infrastructure to support commercialization.

Financial Risk: Kazia is not profitable and may need to raise additional equity or debt capital to support operations, which may negatively impact the stock price. If Kazia is unsuccessful in securing necessary funds, the company may have to delay ongoing trials or scale down its operations.

Dilution Risk: Capital raises to fund operations may dilute investors.

Ownership:
Institutional: 4.3%
Insiders: ~2%

Balance Sheet Summary:
(As of June 30, 2021)
Cash: A$27.6M FY21A
Debt: A$0M FY21A

Analysts covering the stock (*Excluding Maxim Group LLC*): 2 (Buy)

Company Background. Kazia Therapeutics is an innovative oncology-focused biotechnology company based in Sydney, Australia. The company's pipeline includes two clinical-stage drug assets being developed across a range of oncology indications. Licensed from Genentech in late 2016, Kazia's lead program is paxalisib (formerly GDC-0084), a small molecule inhibitor of the PI3K / AKT / mTOR pathway. Paxalisib is being developed for glioblastoma multiforme and various other forms of brain cancers. Paxalisib entered GBM AGILE, a pivotal study in glioblastoma in October 2020. In total, paxalisib is currently in nine active studies. GBM AGILE began recruitment in January 2021. Paxalisib was granted Orphan Drug designation for GBM by the US FDA in February 2018 and Fast Track Designation for GBM in August 2020. In addition, paxalisib was granted Rare Pediatric Disease Designation and Orphan Drug Designation by the FDA for DIPG in August 2020. Kazia is also developing EVT801, a small-molecule inhibitor of VEGFR3, which was licensed from Evotec SE in April 2021. EVT801 is also set to enter the clinic for solid tumors in 2021.

Senior Management:

Iain Ross – Chairman & Non-Executive Director
Mr. Iain Ross was appointed as a non-executive chairman and independent director of the Company in July 2015. Mr. Ross has over 40 years' experience in the international life sciences and technology sectors and has held senior positions at multinational companies including Sandoz AG, Hoffman La Roche, and Celltech Group PLC. He has served as Chairman, CEO, and Director of several biotech companies. He is currently Chairman of Silence Therapeutics plc and ReNeuron Group plc, as well as a non-executive director of Palla Pharma Limited. He is a qualified Chartered Director and former Vice Chairman of the Council of Royal Holloway, London University.

Dr. James Garner – Chief Executive Officer & Executive Director
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 Therapeutics in 2016, he led R&D strategy for Sanofi in Asia-Pacific and was based in Singapore. Dr. Garner is a member of the Australian Institute of Company Directors.

Gabrielle Heaton – Director Finance & Administration
Ms. Heaton has been the Director of Finance since 2017. Prior to Kazia, Ms. Heaton worked extensively in the healthcare sector, and was CFO of a private healthcare group. She is Member of CPA Australia Ltd.

Kate Hill – Company Secretary
Ms. Kate Hill has over 20 years' experience as an audit partner with Deloitte Touche Tohmatsu, working with ASX listed and privately owned clients. She has worked extensively in regulated environments including assisting with Initial Public Offerings, capital raising, and general compliance, as well as operating in an audit environment. Ms. Hill is a member of the Institute of Chartered Accountants in Australia and New Zealand, and a graduate of the Australian Institute of Company Directors.

Steven Coffey – Non-Executive Director
Mr. Coffey was appointed as a Director to the Company in November 2012 and is considered to be an independent Director. Mr. Steven Coffey is a Chartered Accountant, having spent his career in public practice since graduating from NSW University in 1983. He has been a partner in the chartered accounting firm Watkins Coffey Martin since 1993. Mr. Coffey is a registered company auditor and audits a number of large private companies as well as a number of not-for-profit entities.

INVESTMENT SUMMARY

Bull case. Glioblastoma multiforme (GBM), which is characterized by rapid growth and invasion, is the most lethal form of brain cancer that remains largely resistant to treatment. Despite several decades of intensive efforts, no drug has really moved the needle in survival advantage since the introduction of chemotherapy temozolomide (TMZ). Thus, chemo/radiation remains the standard, which only offers 12-21 months of survival. For treating brain cancers, Kazia in-licensed paxalisib, a dual PI3K/mTOR inhibitor from Genentech (RHHBY - NR) in 2016. Bulls view PI3K as an attractive oncology target, as it is upregulated in many cancers, including glioblastoma, where it is upregulated in ~85% of cases. Bulls also readily point out that while PI3K is a validated target, paxalisib is also differentiated from its class, given its ability to cross the blood-brain barrier (BBB) and its (modest) safety profile. With paxalisib, Kazia is first focused on targeting 1L GBM in unmethylated MGMT patients (which is ~65% of GBM patients). In the most recent interim update from the ongoing Phase 2 study, treatment with pax achieved median overall survival (mOS) of 17.5 mos (which compares favorably to TMZ's historical 12.7 mos) and median progression-free survival (mPFS) of 8.4 mos (vs. 5.3 mos TMZ historical). Following this and given paxalisib's clean safety data and promising clinical activity in the brain, Kazia was invited (as one of three biotech/pharma partners) to join the novel, platform physician led GBM AGILE study in 2020. Furthermore, paxalisib has garnered attention from leading scientists in the space, resulting in the initiation of multiple investigator-sponsored trials with paxalisib being explored in different CNS-based tumors (brain metastases, DIPG). Combined, Bulls would note that paxalisib is now set to be evaluated in 9 clinical trials to date. In addition to paxalisib, Kazia has a second asset, EVT801, a novel VEGF receptor inhibitor, in-licensed in April 2021 from Evotec (EVT.DE - NR) for solid tumors. For Bulls, both of Kazia's two product candidates are two de-risked clinical targets (PI3K and VEGF) that could each offer blockbuster opportunities. Overall, given the size of the potential markets, with a market capitalization of ~$140M today, success is not yet factored in, and Bulls see upside.

Bear case. The company is primarily dependent on its PI3K drug candidate for its valuation. Although both in-licensed drug candidates from Kazia's pipeline are from two validated class of drugs (PI3K and VEGFR), Bears would remind that the PI3K class has struggled to make an impact on the market. The first PI3K launched by Gilead, idelalisib, never reached the expected blockbuster levels due to its toxicity profile. Others that have followed since, such as duvelisib and copanlisib, have also demonstrated disappointing safety profiles. Although Kazia's drug has shown clinical activity and modest safety in a Phase 2b study in newly diagnosed GBM patients, Bears may note the small cohort size (n=24). Accordingly, Bears may not find the data to date sufficient and thus may be more cautious on drawing direct comparisons to historical controls as a benchmark. Further, there is no guarantee that paxalisib will demonstrate a superior clinical profile in the randomized, controlled pivotal GBM AGILE study. As such, Bears may see risk in pursuing GBM. Drug development in this setting has been notoriously difficult, which has included many high-profile failed studies such as Bristol's (BMY - NR) CheckMate-498 and CheckMate-548 with nivolumab. Finally, data on the company's follow-on candidate, EVT801, is all very early (preclinical), which presents additional risk to Bears.

Our take. Checkpoint inhibitors (CPI) have revolutionized the field of cancer therapy and have seen unprecedented success in many tumor types (metastatic melanoma and lung cancer, to name a few). However, one setting where CPIs have seen limited benefit is GBM, a well-known heterogeneous "cold tumor" with an immunosuppressive microenvironment. Given that GBM continues to show resistance to nearly most therapies, with little progress made in improving patient prognosis in the past few decades, development of more effective therapies, potentially targeted therapies, are urgently needed. PI3K is upregulated in GBM but despite the importance of the pathway, few agents inhibiting this signaling pathway have been able to adequately cross the blood–brain barrier or show efficacy in brain cancers. Kazia's paxalisib was specifically engineered to penetrate the BBB and has demonstrated promising single agent activity in an ongoing P2 study in 1L GBM patients (a survival benefit of ~5 months with the drug over historical control). While most of the five currently approved PI3K inhibitors have not achieved commercial success owing to their safety profile, safety from paxalisib has been positive; and the drug has not shown any safety signals to date. Given its potential clinical efficacy in CNS-based tumors, paxalisib has also garnered considerable traction among clinical investigators at prominent academic institutions across the US, resulting in the initiation of multiple investigator-sponsored clinical trials as well as an invitation to join the groundbreaking P2/3 GBM AGILE trial. In total, paxalisib has entered an impressive 9 trials, joining GBM AGILE in 4Q20. In our view, GBM AGILE offers Kazia multiple advantages: speed (given the existing infrastructure), reduction in cost (with funding from grants), involvement of key opinion leaders, and regulatory endorsement. We believe that the platform study will help Kazia to efficiently generate clinically meaningful results, which, if positive, can provide Kazia an expedited path to registration in several large markets (North America, EU, China, potentially in late 2024). Taken together, we are optimistic for the drug's success in the pivotal GBM AGILE trial. However, Kazia's story does not end with paxalisib.

In an effort to expand its pipeline, Kazia brought in a VEGF signaling inhibitor in April 2021, EVT801. While VEGF inhibitors have been one of the most successful approaches to the treatment of cancer (e.g., Avastin), many ultimately face tumor resistance. It is believed that EVT801, given its slightly differentiated mechanism of action, may be able to avoid this problem. EVT801 is set to enter the clinic by year end, in 2021. In the near term, Kazia has several study readouts (interim and final) from its ongoing paxalisib studies in the fourth quarter, beginning at SNO (Society for Neuro-Oncology in November). Altogether, we see in Kazia's pipeline two de-risked clinical targets (PI3K and VEGF) with potentially improved pharmacology and better safety profile that may be able to address multiple tumor types. GBM alone is a multibillion-dollar space; thus, at a market cap of only ~$140M, success is yet not factored in. With ~$20M (A$27.6M) on the balance sheet, and with paxalisib's participation in the GBM AGILE (to reduce costs), Kazia is well funded to reach multiple catalysts; and as the data emerge, we expect a higher valuation.

Finances. On August 26, 2021, Kazia Therapeutics reported FY2021(June YE) with revenue of $11M (A$15.2M) through partnering activities. Kazia reported a net loss of ($6.1M or A$8.4M) and ended the period with ~$20M (A$27.6M) in cash on the balance sheet (no debt). This

includes an equity raise in October 2020, whereby the company raised ~$17.4M (A$24M) in gross proceeds. With a monthly burn of ~$1.25M we estimate Kazia is funded through mid-CY22, though we do expect expenses to increase with EVT801 Phase 1 study initiating. As a microcap biotechnology company, Kazia will still likely need to raise capital to continue funding operations over time, which we factor into our model.

Exhibit 1. Upcoming catalysts.

Product	Indication	Event	Timeline	Impact
Paxalisib	GBM	Final P2 data at SNO	4Q21	++
Paxalisib	DIPG	Initiate PNOC (IST) paxalisib combination study	4Q21	+
Paxalisib	BCBM	Initial interim P2 brain mets data at Dana Farber (IST)	4Q21	++
Paxalisib	Brain Mets	Initial interim P2 brain mets data by Alliance Group	4Q21	++
Paxalisib	Brain Mets	Initial interim P1 brain mets data at Sloan-Kettering	4Q21	++
EVT801	Solid tumors	Initiate P1 study	4Q21	+

Stock Significance Scale: + of moderate importance; ++ higher level; +++ very important

Source: Company Reports and Maxim Forecasts.

Exhibit 2. Pipeline.

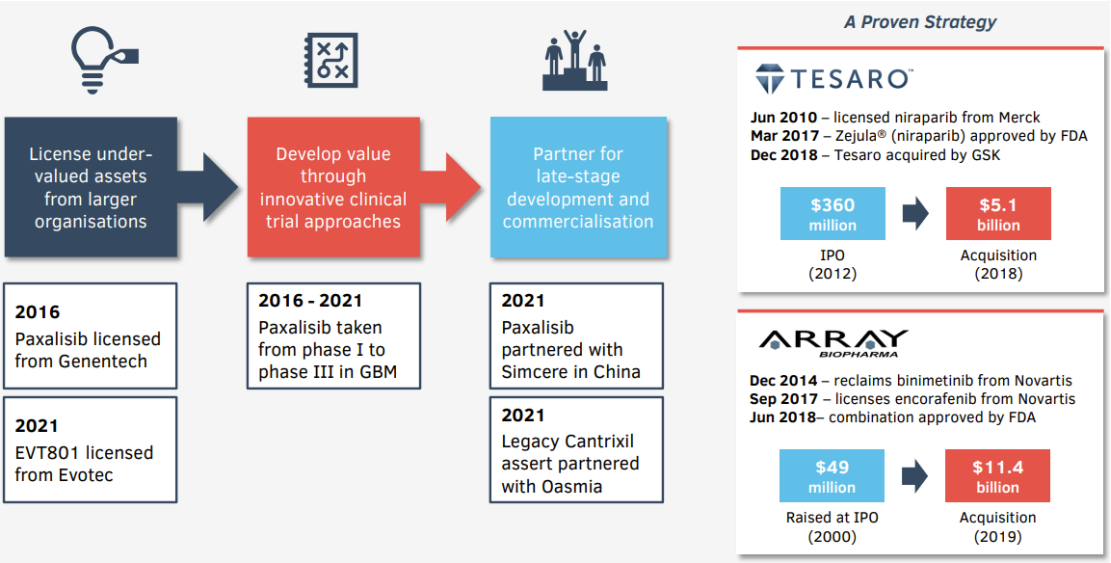
Product	Indication	Development	Pre-IND	Phase I	Phase II	Phase III
Paxalisib (PI3K/mTOR)	Glioblastoma (AGILE)					
Paxalisib (PI3K/mTOR)	DIPG (IST)					
Paxalisib (PI3K/mTOR)	Primary CNS Lymphoma (IST)					
Paxalisib (PI3K/mTOR)	Brain Metastases (IST)					
EVT801 (VEGFR3)	Solid Tumors					

Source: Company Reports and Maxim.

Kazia's Business Strategy

Strategy. Kazia has taken a strategy of pipeline growth and expansion via in-licensed deals, rather than expending internal resources on drug discovery and preclinical R&D. In doing so, the company expects to drive value earlier by bringing on board clinic-ready assets (such as paxalisib in 2016 and EVT801 in 2021). We see some parallels between Kazia's strategy for drug development to Tesaro's. Tesaro, for instance, in-licensed PARP inhibitor, Zejula (niraparib), from Merck (MRK - NR), that the company saw to FDA approval in 2017. The company was then acquired by GlaxoSmithkline (GSK - NR) in 2018 for $5.1 billion. Zejula generated £339 million (~$462M) in revenue in 2020 for GSK.

Exhibit 3. Kazia's operating model – a proven strategy. In-licensing advanced assets can drive value realization earlier, as seen with some biotechs in recent past such as Tesaro and Array. Both were subsequently acquired by large pharma.



Source: Company reports.

Paxalisib

On October 2016, Kazia (then Novogen) in-licensed Phase 2-ready paxalisib (GDC-084, small molecule inhibitor of PI3K/AKT/mTOR pathway) from Genentech, after the drug had demonstrated signals of efficacy in a Phase 1 safety study in patients with advanced brain cancer. Kazia paid an upfront of $5M. In addition, Genentech could receive regulatory and commercial milestones, plus royalties in-line with industry benchmarks.

EVT801

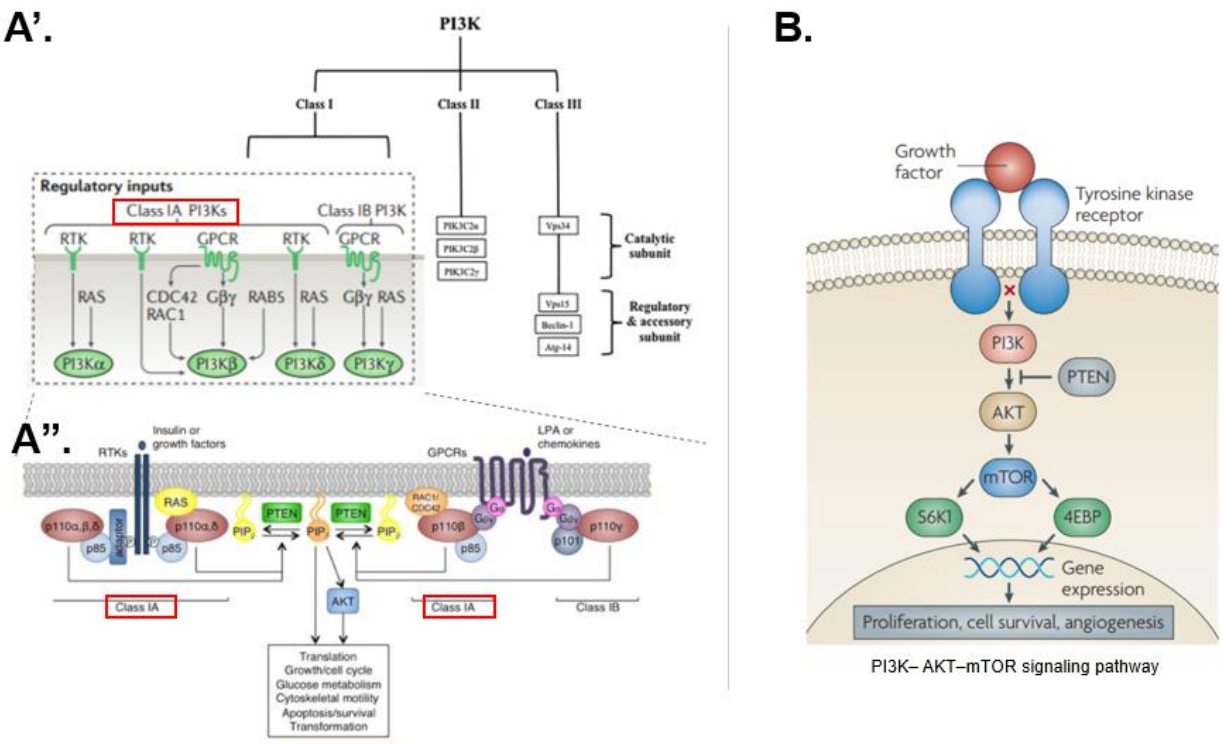
On April 19, 2021, Kazia announced an in-licensed deal from Evotec (EVT.DE - NR) under which it had acquired the world-wide rights to develop, manufacture, and commercialize EVT801 (VEGFR3 inhibitor) in all indications. Kazia and Evotec also entered into a master services agreement, under which the two companies will continue to collaborate on further development of EVT801. EVT801 is expected to enter the clinic in a Phase 1 study in 2021. As part of the agreement, Kazia paid an upfront ~$1.16M (€1 million). Kazia may also pay contingent milestones of up to ~$347M million (€300 million) related to achievement of clinical, regulatory, and commercial outcomes over the lifetime of the drug, and a tiered single-digit royalty on net sales.

Paxalisib: A Top PI3K for Brain Cancers

PI3Ks are critical coordinators of intracellular signaling. The PI3K/AKT/m-TOR signaling pathway coordinates various vital functions, including cell growth, proliferation, differentiation, metabolism, and angiogenesis.[1] Inappropriate hyperactivation of the Phosphatidylinositol-3 kinase (PI3K) pathway can contribute to cancer progression and immune disorders. To that end, the Cancer Genome Atlas (TCGA) has identified the PI3K pathway as one of the most frequently altered pathways in human malignancies and cancer progression.[2] Mutations and amplifications in the pathway account for about 30%-50% of human tumors, and, more specifically, in > 80% of human glioblastomas.[2,3] Altogether, PI3K has been implicated in ovarian, breast, prostate, gastric, colorectal, glioblastoma, lymphomas, endometrial, and brain cancers.[3,4] Hence, the ability to effectively inhibit the signaling pathway has made it an attractive drug target across multiple tumor types.

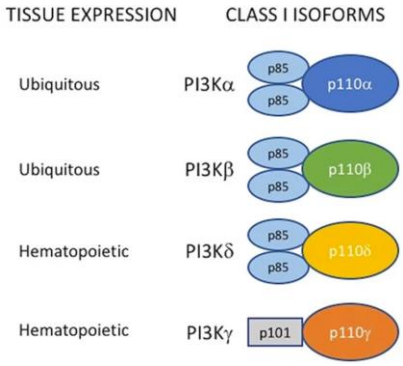
Exhibit 4. The PI3K family overview and signaling. PI3Ks belong to a large family of signaling kinases (enzymes) that produce lipid second messengers to regulate intracellular signaling. At the cellular level, PI3K functions in the PI3K/AKT/m-TOR signaling pathway and contributes to cell growth, differentiation, and survival, and is frequently dysregulated in diverse pathologies (such as cancer, metabolic disorders, neurodegeneration, and aging).[3] **(A')** The broader PI3K super family are divided into three main classes (I, II, and III) based on their molecular structure, function, and substrate specificity.[5] In total, there are eight PI3K isoforms. Of these, class I is the most implicated in human cancer.[4] The class I PI3K family is further divided into two subclasses: class IA isoforms PI3K-α, -β, -δ (alpha, beta, delta) and the class IB isoform PI3K-γ (gamma). Class II and III are not as well defined. **(A")** Activation of the PI3K pathway begins with growth factors or cytokine receptors binding to receptors at the cell surface (i.e., GPCR, RTKs). This causes activation of class I PI3K, which it facilitates the production of the second-messenger molecule, PIP3.[4] **(B)** Increased levels of PIP3, in turn, directly activates effector signal transduction pathways via AKT. Completing the signaling cascade is mTOR, which is composed of two functionally distinct complexes: mTORC1 and mTORC2. Some consider mTOR as class IV of PI3K-related kinase. As global inhibition of PI3Ks would likely to be deleterious, pharmacological inhibition of PI3K signaling has explored drugs that target specific (or groups of) PI3K isoforms as well as downstream molecules.

[1] Thorpe LM et al., Nat Rev Cancer. 2015; 15(1):7-24.
[2] Brennan CW et al., Cell. 2013; 155(2):462-477.
[3] Elmenier FM et al., Eur J Med Chem. 2019; 183:111718.
[4] Bauer TM et al., Pharmacol Ther. 2015; 146:53-60.
[5] Lai K et al., J Clin Pathol. 2015;68(4):253-257.



Source: Modified Lai K et al.,2015; Bilanges B et al., 2019; Thorpe LM et al., 2015.

Exhibit 5. PI3K tissue distribution.[6] PI3Kα and PI3Kβ are ubiquitously expressed (i.e., found in all cell types). PI3Kα is involved in insulin signaling, angiogenesis, and often found to be mutated in solid tumors. PI3Kβ is involved in platelet function. By contrast, PI3K-γ expression is largely restricted to leukocytes (white blood cells; and thus, in white blood cell function. PI3Kγ, is abundantly expressed in immune cells of myeloid origin (e.g., macrophages, monocytes), which regulate innate immunity in inflammation and cancer.[7] PI3Kγ has also been implicated in the maintenance of the tumor microenvironment.[4] PI3Kδ plays an important role in B-cell receptor development, survival of B cells, and is known to be hyperactive in many B cell malignancies. While PI3Kα, β and δ are growth factor receptor and/or cytokine dependent, PI3K-γ activation is driven by the activation of G-protein coupled receptors (GPCRs), many of which function as chemokine receptors.



Source: Modified Visentin A et al., 2020.

PI3Ks are a validated target but most have been plagued by safety issues. Enormous efforts have been dedicated to the development of effective PI3K inhibitors for cancer therapy. In January 2021, the fifth product in the PI3K inhibitor class was approved by the FDA – TG Therapeutics' (TGTX - NR) umbralisib for refractory lymphomas. Of note, the approval was preceded by an award of breakthrough designation for the drug, which, in our view, illustrates the growing significance of the PI3K class in the cancer armamentarium, since Kazia licensed its lead asset, dual PI3K/mTOR inhibitor (paxalisib), from Genentech back in 2016. Once viewed as blockbuster opportunities, particularly in heme malignancies, PI3Ks subsequently seemed to enter the penalty box following a host of toxicities as well as deaths with the first approved PI3K

[6] Okkenhaug & Vanhaesebroeck B. Nat. Rev. Immunol. 2003 3(4): 37-330.
[7] Yang J et al., Mol Caner. 2019;18(1):26.

inhibitor, (Zydelig) when it was tested in the frontline setting. However, more recently, the approvals of umbralisib and alpelisib, and even promising results from the pan-PI3K inhibitor copanlisib, in combination with rituxan showing safety and improved efficacy in indolent non-Hodgkin's lymphoma (iNHL) may have begun to redeem the class.

Exhibit 6. The PI3K class is well established. Currently, there are five PI3K inhibitors on the market, most of which block the δ isoform and are targeted towards heme malignancies. However, there have been some limitations to their uptake and commercial success such as drug-related toxicities and increase in insulin production from systemic inhibition (from feedback upregulation of compensatory mechanisms). Consequently, the first three drugs to reach the market especially (idelalisib, copanlisib and duvelisib) have not been used extensively.

Company	Drug	Primary MOA	IC50 (nM)					Status	Indication
			α	β	δ	γ	mTOR		
Gilead	Zydelig (idealisib)	PI3Kδ	820	565	2.5	89	>1000	Approved	Relapsed chronic lymphocytic leukemia (CLL) in combination with rituxumab, relapsed follicular B-cell non-Hodgkin lymphoma (FL), relapsed small lymphocytic lymphoma (SLL)
Bayer	Aliqopa (copanlisib)	PI3Kα/δ	0.5	3.7	0.7	6.4	45	Approved	Relapsed follicular lymphoma
Verastem	Copiktra (duvelisib)	PI3Kδ/γ	1602	85	2.5	27.4		Approved	Relapsed chronic lymphocytic leukemia or small lymphocytic lymphoma (SLL)
Novartis	Piqray (alpelisib)	PI3Kα	5	1200	250	290	>9100	Approved	PIK3CA mutation in HR+/HER2- advanced breast cancer
TG Therapeutics	Ukoniq (umbralisib)	PI3Kδ/CK1ε	>10,000	1116	22	1065		Approved	Relapsed follicular lymphoma, refractory marginal zone lymphoma (MZL)
Roche (Genentech)	pictilisib (GDC-0941)	PI3Kα/δ	3	33	3	75	580	Discontinued	
Kazia Therapeutics	Paxalisib (GDC-0084)	PI3Kα/mTOR	2	46	3	10	70	Phase III	GBM, brain cancers, brain mets

Source: Company reports and Maxim Group research.

Classifications of PI3K inhibitors. PI3K inhibitors can be largely divided into three categories according to selectivity: pan-PI3K inhibitors, isoform-specific inhibitors, and dual PI3K/mTOR inhibitors.

Pan-PI3K:

- **Aliqopa (copanlisib/BAY80-6946)** - Bayer (BAYRY- NR). Copanlisib is a pan-PI3K intravenous inhibitor with IC50: 0.5, 3.7, 6.4, 0.7 nM against PI3Kα, β, δ and γ isoforms, respectively.[3] The drug has predominant activity against the α and δ isoforms. Copanlisib was approved on September 14, 2017, for adult relapsed follicular lymphoma patients.[8] Copanlisib is approved for various forms of non-Hodgkin lymphoma (NHL). With the exception of copanlisib, PI3K inhibitors that have targeted all isoforms have suffered from toxicities as well as insufficient efficacy, leading to their discontinuations.

Compared to pan-PI3Ks, more specific PI3K inhibitors (either selective inhibitors or dual inhibitors) are expected to limit toxicities like immune suppression and glucose tolerance while improving tolerability.

Selective isoform inhibitors:

- **Zydelig (idelalisib/CAL-101)** - Gilead (GILD - Buy). Idelalisib was the first drug approved in its class. Gilead acquired idelalisib when it bought Seattle-based Calistoga Pharmaceuticals in February 2011 for ~$600M.[9] Zydelig is an oral twice daily, selective PI3Kδ inhibitor with an IC50 value of 2.5 nM. It was approved by FDA in July of 2014 for patients with relapsed chronic lymphocytic leukemia (CLL), follicular lymphoma (FL) and small lymphocytic leukemia (SLL).[10] Of importance, following a series of adverse events and deaths in clinical studies in first-line patients, the FDA and EMA conducted safety reviews in 2016, which resulted in the termination of multiple clinical studies. In clinical trials, the drug was associated with 20%-50% discontinuations. As such, Zydelig's label carries a Black-Box Warning for the risk of fatal and serious AEs. Gilead posted idelalisib net sales of $133 million, $103 million, $72 million in 2018, 2019, 2020, respectively.
- **Ukoniq (umbralisib/TGR1202)** - TG Therapeutics' umbralisib is a potent, next-generation PI3Kδ inhibitor, which has an improved toxicity profile to idelalisib and duvelisib (described below, Exhibit 7). In addition, umbralisib has a significant effect on the protein, casein kinase-1 epsilon (CK-1ε), which plays an inhibitory role on regulatory T-cell function and is involved in the translation of c-Myc as well as the regulation of the Wnt5a (a known actor of PI3K-induced colitis).[11] In February 2021, umbralisib was granted accelerated approval for marginal zone lymphoma (MZL) and follicular lymphoma.[12] The drug generated $2.3 million in revenue from launch through the end of 2Q21 (~4 months).

[8] FDA.gov. Aliqopa (copanlisib) approval: "FDA approves new treatment for adults with relapsed follicular lymphoma"
[9] Allison M. Nat Biotech. 2013; 31:90.
[10] Gilead press release: "U.S. Food and Drug Administration Approves Gilead's Zydelig® (idelalisib) for Relapsed Chronic Lymphocytic Leukemia, Follicular Lymphoma and Small Lymphocytic Lymphoma"
[11] Visentin A et al., Onco Targets Ther. 2020; 13:9679-9688.
[12] FDA.gov. umbralisib approval: "FDA grants accelerated approval to umbralisib for marginal zone lymphoma and follicular lymphoma"

- **Piqray (alpelisib/BYL719)** - Novartis (NVS - NR). Alpelisib is a next-gen, oral selective PI3Kα isoform inhibitor. Alpelisib was approved (May 2019) in combination with fulvestrant for postmenopausal women, and men, with hormone receptor (HR)-positive, human epidermal growth factor receptor 2 (HER2)-negative breast cancer with a PIK3CA mutation.[13] Alpelisib is also under development for use in triple negative breast cancer and HER2-positive advanced breast cancer.

Dual PI3K inhibitors

- **Copiktra (duvelisib/IPI-145)** - Verastem (VSTM - NR). In November 2016, Verastem licensed duvelisib from Infinity Pharmaceuticals (INFI - NR) for $28 million in milestones. Duvelisib is a second-generation oral, BID, dual inhibitor of PI3Kδ and γ that was approved on September 24, 2018, for the treatment of relapsed/refractory chronic lymphocytic leukemia or small lymphocytic lymphoma.[14] The drug also received accelerated approval in FL. While duvelisib-mediated PI3Kδ inhibition blocks cancer cell survival pathways downstream of the b-cell receptor, targeting of PI3Kγ appears to inactivate the immune cells within the tumor microenvironment (where PI3Kγ is more commonly expressed, aiding CLL cells in proliferation and migration via the activities of T lymphocytes and macrophages.[11] While dual PI3Kγ/δ inhibitors have a broader effect than inhibition of either isoform alone, a key challenge is controlling the balance of activity between the two isoforms. Additionally, greater mechanism-based side effects can be a potential issue.

Paxalisib (formerly GDC-0084) is a dual class I PI3K/mTOR inhibitor. In addition to the three categories of PI3K inhibitors, some have also explored the development of dual PI3K/mTOR inhibitors. Kazia's lead product candidate, paxalisib, falls under this category. Paxalisib is an oral, small molecule, bioavailable, molecule inhibitor of the PI3K pathway that was in-licensed from Genentech, a subsidiary of Roche, in 2016. With a PI3K/mTOR drug, the thought is that dual inhibition may not only offer the benefits of better efficacy (by potentially fully blocking signaling through the entire pathway) but may also help overcome the resistance problem that arises with selective isoform inhibitors.[4]

Exhibit 7. Though currently approved PI3K drugs are very active, safety is a common problem. Several of the approved agents target PI3Kδ (idelalisib, copanlisib, duvelisib). While these drugs have demonstrated therapeutic benefit, most of them have been limited by their side-effect profile (e.g., severe infections, colitis and other gastrointestinal effects). Thus, common AEs have created a narrow therapeutic window for the class.[4] In contrast, Kazia's paxalisib, which inhibits the α isoform in addition to mTOR, has shown a modest safety profile in the ongoing Phase 2 study in newly diagnosed glioblastoma patients, which, in our view, is very encouraging.

[13] FDA.gov. alpelisib approval: "FDA approves alpelisib for metastatic breast cancer"
[14] FDA.gov. duvelisib approval: "duvelisib (COPIKTRA, Verastem, Inc.) for adult patients with relapsed or refractory chronic lymphocytic leukemia (CLL) or small lymphocytic lymphoma (SLL)"

	Zydelig (idealisib)	Aliqopa (copanlisib)	Copiktra (duvelisib)	Piqray (alpelisib)	Ukoniq (umbralasib)	paxalisib
Crosses BBB	x	x	x	x	x	√
Patients	N=110	N=317	N=442	N=284	N=335	N=24, P2 study in GBM
Dosing	150mg BID, PO	60mg, IV (1hr)	25mg BID, PO	300mg QD, PO	800mg QD, PO	60mg BID, PO
Safety	**Black Box Warnings**	**Warnings and Precautions**	**Black Box Warnings**	**Warnings and Precautions**	**Warnings and Precautions**	
Stage	**Approved**	**Approved**	**Approved**	**Approved**	**Approved**	**Phase 3**
Hepatotoxicity (ALT and/or AST Elevations)	• **Fatal and/or serious hepatotoxicity** occurred in **16% to 18%** of Zydelig treated patients		• Hepatotoxicity (≥Gr 3 ALT 8%; ≥Gr 3 AST 2%)		• **Hepatotoxicity** (≥Gr 3 8%+)	
Diarrhea	• **Fatal and/or serious and severe diarrhea or colitis** occurred in **14% to 20%** of Zydelig-treated patients (All Gr, 55%)	• Diarrhea (All Gr, 36%; Gr 3, 4%; n=168)	• **Fatal and/or serious diarrhea or colitis occurred in 18%** of COPIKTRA-treated patients	• **Severe cases of diarrhea** (All Grades, 58%;Gr 3, 7%)	• **Diarrhea or non-infectious colitis** (All Grades 53% A; ≥Gr 3, 9%)	• Diarrhea (All Gr, 25%; ≥Gr 3, 0%)
Pneumonitis	• **Fatal and/or serious pneumonitis** occurred in 4% of Zydeligtreated patients	• **Non-infectious pneumonitis (NIP, 5%)**	• **Fatal and/or serious pneumonitis occurred in 5%** of COPIKTRAtreated patients	• **Severe cases of pneumonitis** (1.8%)	• Upper respiratory tract infection (All Gr, 21%; ≥Gr 3, <1%, n=221)	
Infections	• **Fatal and/or serious infections occurred in 21% to 48%** of Zydelig-treated patients	• **Infections** (19%)	• **Fatal and/or serious infections occurred in 31%** of COPIKTRA treated patients		• **Infections** (≥Gr 3, 10%)	
Cutaneous Reactions; Rash	• Rash (All Gr 25%; ≥3, 4%)	• **Severe cutaneous reactions** (≥Gr 3, 2.8%); rash (All Gr, 15%; ≥Gr3, 1%, n=168)	• **Fatal and/or serious cutaneous reactions occurred in 5%** of COPIKTRA-treated patients	• **Severe cutaneous reactions**; rash (All Gr, 18%)	• **Severe cutaneous reactions** (Gr 3, 2%)	• Rash (All Gr, 71%; ≥Gr 3, 29%)
Perforation	• **Fatal and serious intestinal perforation**					
Fatigue	• Fatigue (All Gr, 34%)	• Fatigue (All Gr, 36%; ≥Gr 3, 4%, n=168)	• Fatigue (All Gr, 29%; ≥Gr 3, 5%)	• Fatigue (2.5%)	• Fatigue (All Gr, 41%; ≥Gr 3, 3%, n=221)	• Fatigue (All Gr, 58%; ≥Gr 3, 8%)
Hyperglycemia		• **Hyperglycemia** (≥Gr 3, 41%)		• **Severe hyperglycemia** (All Grades, 65%; ≥Gr 3, 33%+)		• Hyperglycemia (All Gr, 33%; ≥Gr 3, 21%)
Hypertension		• **Hypertension** (Gr 3, 26%)				
Hypersensitivity	• Serious hypersensitivity reactions			• **Severe hypersensitivit** (≥Gr 3, 0.7%)	• **Allergic reactions due to inactive ingredient** FD&C Yellow No. 5	• Drug reaction (≥Gr 3, 13%)
Embryo Fetal Toxicity	• Embryo fetal toxicity (may cause)	• Embryo fetal toxicity	• Embryo fetal toxicity	• **Embryo fetal toxicity**	• **Embryo fetal toxicity**	
Neutropenia	•Neutropenia(≥Gr3, 25%)	•Neutropenia(≥Gr3, 24%)	•Neutropenia (≥Gr 3, 42%)		• Serious neutropenia (≥Gr 3, 9%)	•Decreased neutrophils (All Gr, 25%; >Gr 4, 4%)
	Potentially fatal liver toxicity and diarrhea	Potentially fatal infections	Potentially fatal infections and diarrhea	Modest toxicities to date	Serious infections, hepatotoxicity, diarrhea	Modest toxicities to date

Source: Company reports & Maxim Group research.

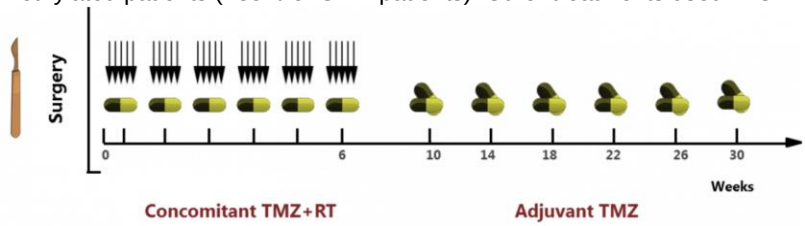
Glioblastoma multiforme

PI3K is altered in GBM. Glioblastoma multiforme (GBM) is a complex, invasive, and aggressive disease with a dismal prognosis. GBM is the most frequently diagnosed primary brain tumor in adults, accounting for more than 10,000 patients each year in the United States.[15] Once GBM is diagnosed, median survival is less than 2 years.[15] The total annual cost of caring for patients with metastatic CNS disease exceeds $10 billion in the US alone.[16] Aberrant PI3K signaling has been associated with more than 80% of GBM cases.[17] Thus, this pathway represents a compelling target for the treatment of the disease.

Treatment options of GBM are limited. Current (aggressive) treatment of resection, followed by radiotherapy combined with temozolomide plus adjuvant temozolomide (i.e., Stupp regimen) with or without tumor-treating fields, yields only 12-21 months of clinical benefit, which is seen in predominantly patients with unmethylated MGMT promoter status (~35% of GBM patients).[5] Methylated MGMT (methylguanine methyltransferase) status is associated with improved outcome. Only 5% of patients survive longer than five years.[15] Almost all patients relapse after first-line treatment failure, leaving limited treatment options for glioblastoma patients.

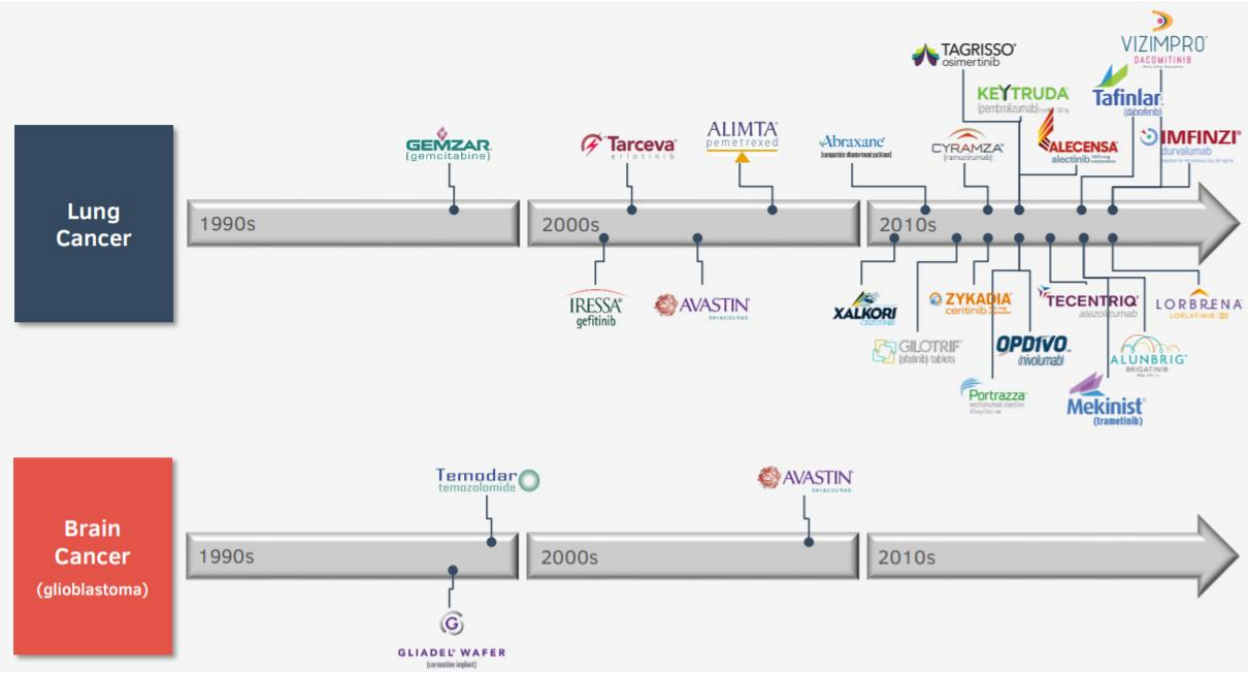
[15] Salphati L et al., Drug Metab Dispos. 2016; 44(12):1881-1889.
[16] Alliance for Clinical Trials in Oncology A071701: Genomically-guided treatment in brain metastases.
[17] The Cancer Genome Atlas Network. Nature 2008, 455, 1061−1068.

Exhibit 8. Standard of care - Stupp regimen. The standard of care for patients diagnosed with GBM is surgical resection, where the neurosurgeon removes as much of the tumor as possible. This is followed by concomitant daily radiation (RT) and oral chemotherapy (temozolomide) for six and a half weeks, then a six-month regimen of oral chemotherapy. Temozolomide (TMZ) is more effective in MGMT methylated patients (~35% of GBM patients). Other treatments used in GBM include Gliadel wafers and Tumor treating fields (TTF).



Source: Precision Cancer Medicine Group.

Exhibit 9. Treatment of brain cancer has improved little in the last few decades. Unlike other cancers such as lung cancer, there have been few advances in GBM drug development in the past decades. Most drugs, including PI3K inhibitors have not demonstrated any convincing evidence of an ability to improve overall survival (OS) in GBM to date.



Source: Company reports.

Exhibit 10. Approved therapies in GBM (high grade gliomas). Outside of temozolomide, there are four drugs and one device that are FDA-approved for the treatment of GBM: lomustine, intravenous carmustine, carmustine wafer implants, bevacizumab, and tumor treatment fields. Only TMZ, tumor treating fields and carmustine wafer implants are approved for new diagnoses. All high-grade gliomas eventually progress and there is no standard of care for recurrences.

Agent	Company	Application	Indication	Mechanism	Safety (Common toxicities)	Clinical data (Overall Survival)
Temodar (temozolomide)	Merck	Oral	All (soc)	Alkylating agent that causes mismatch repair in DNA by methylation at the O6 position of guanine	Hematologic toxicity (16%): thrombocytopenia (12%), leukopenia (7%), and neutropenia (7%)	14.6 -16.1 mos
Avastin (bevacizumab)	Roche	IV	Recurrent	Binds and inhibits VEGF	Hypertension (5.5–11.4%), thromboembolic events (3.2–11.9%), gastrointestinal perforation (1.5–5.4%), cerebral bleeding (2–5.3%), wound healing complications (0.8–3.3%), and proteinuria (2.7–11.4%)	9.3 mos (recurrent)
Carmustine (BiCNU)	Emcure Pharmaceuticals	IV	Recurrent	Alkylating agent that causes crosslinking of DNA and RNA in dividing cells; also binds to and modifies glutathione reductase	Pulmonary toxicity (<30%), ocular toxicity (>10%) and bone marrow suppression (>10%)	11.75 mos
Gliadel wafer (Carmustine wafers, BCNU)	Arbor Pharmaceuticals	Directly applied during surgery	Recurrent and new	Alkylating agent that causes crosslinking of DNA and RNA in dividing cells; also binds to and modifies glutathione reductase	Wound healing complications (12%), intracranial infection (1–10%), and cerebral edema (1–10%)	13.9 mos
Gleostine (lomustine)	NextSource Biotechnology	Oral	Recurrent	Alkylating agent that causes crosslinking of DNA and RNA in dividing cells triggering cell death	Hematologic toxicity (49.7%)	11.5 mos OS
Optune device (TTFields)	Novocure	Portal device, electrodes on scalp	Recurrent and new	Low-intensity, intermediate frequency (200 kHz) alternating electric fields that disrupt mitosis in tumor cells	Skin toxicity (43%) and seizures (7%)	20.5–20.9 mos

Source: Fisher JP et al., 2021.

Paxalisib was designed to cross the blood-brain barrier. Despite the importance of the PI3K/mTOR pathway in glioblastoma, few agents inhibiting this pathway have been able to adequately cross the blood-brain barrier or show efficacy in brain cancers. Hence, most clinical trials targeting this pathway have failed to date.[19] Kazia's paxalisib (GDC-0084) is a potent, oral, brain-penetrant small-molecule inhibitor of PI3K and mTOR that targets altered tumor vascularity and metabolism, respectively.[18] Paxalisib was specifically designed and optimized to efficiently cross the BBB, to exhibit metabolic stability in the body, and to achieve high drug exposure in order to maximize its potential to treat central nervous system (CNS) tumors.[18,19] While paxalisib is active against all four isoforms of PI3K (α, β, γ, and δ), it has the greatest affinity for the PI3Kα isoform (K_i 2 nM); it also has activity against mTOR (K_i 70 nM). Currently, paxalisib is being evaluated in patients, following promising preclinical studies.

Exhibit 11. Positioning paxalisib for success with a broad clinical development strategy in CNS tumors. Given promising preclinical and early clinical data, paxalisib is presently being evaluated in nine clinical trials in multiple forms of brain cancer, including the groundbreaking pivotal GBM AGILE trial.

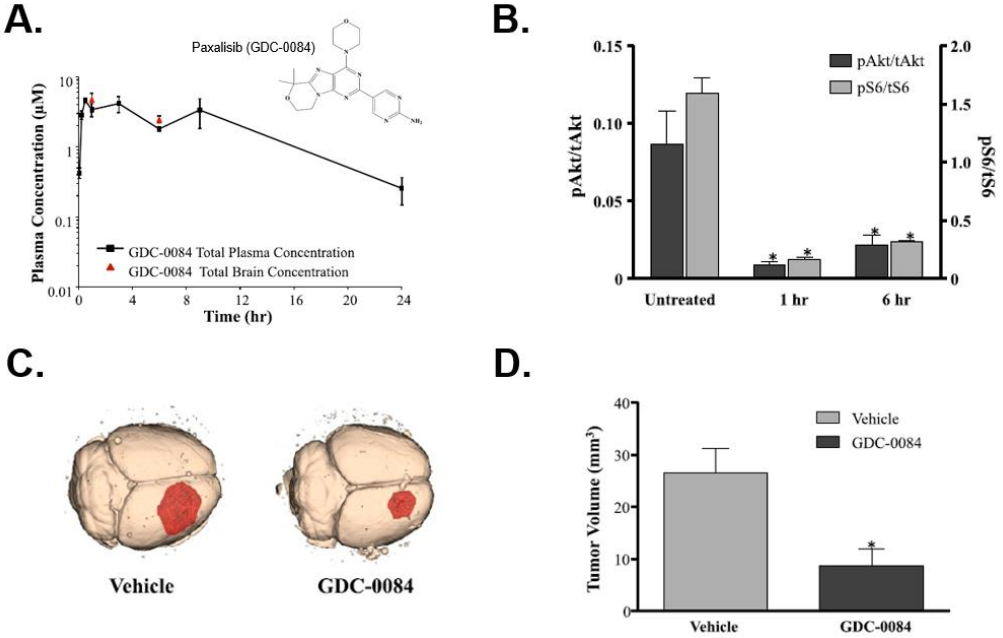
[18] Heffron TP et al., ACS Med Chem Lett. 2016; 7(4):351-356.
[19] Salphati L et al., Drug Metab Dispos. 44(12):1881-1889.

Registration	Indication	Phase	N	Status	Sponsor
Primary Brain Cancer					
NCT03522298	Glioblastoma	II	30	Follow-up	KAZIA THERAPEUTICS
TBD	Glioblastoma (combination with ketogenic diet)	II	33-60	Start-up	Weill Cornell Medicine
NCT03970447	Glioblastoma (GBM AGILE)	II / III	Up to 200 on paxalisib	Recruiting	GLOBAL COALITION FOR ADAPTIVE RESEARCH
NCT03696355	DIPG and DMGs	I	27	Follow-up	St. Jude Children's Research Hospital
TBD	DIPG and DMGs	II	TBD	Start-up	Pacific Pediatric Neuro-Oncology Consortium
NCT04906096	Primary CNS Lymphoma	II	25	Recruiting	DANA-FARBER CANCER INSTITUTE
Secondary (Metastatic) Brain Cancer					
NCT04192981	Brain Metastases (combination with radiotherapy)	I	Up to 36	Recruiting	Memorial Sloan Kettering Cancer Center
NCT03765983	Breast Cancer Brain Metastases (combination with trastuzumab)	II	Up to 47	Recruiting	DANA-FARBER CANCER INSTITUTE
NCT03994796	Brain Metastases ('Alliance' multi-drug study)	II	50	Recruiting	NIH NATIONAL CANCER INSTITUTE

Source: Company reports.

Preclinical work

Exhibit 12. Efficacy in mouse tumor models of GBM – paxalisib (GDC-0084) can cross the BBB and block PI3K. [20] Paxalisib was optimized to cross the blood-brain barrier and has single agent activity in preclinical models. Paxalisib treatment can block proliferation of several glioma cell lines in vitro (not shown), penetrate within intracranial tumors and distributes readily in the brain and engages its target where intended (shown). **(A)** CNS penetration in a mouse model – paxalisib is able to freely cross the BBB following PO (by mouth) administration (25 mg/kg). **(B)** Quantification of western blots of mouse brains – levels of free drug (i.e., available to interact with PI3K in the brain) achieves significant suppression, as demonstrated by reduction of pAkt/total Akt and pS6/total S6 at 1- and 6-hours post-dose in CD-1 mice. Akt is a key signal within the PI3K pathway. **(C, D)** Paxalisib administration can significantly reduce tumor volumes (~70%) in an orthotopic model of GBM (U87 model), compared with the vehicle control. Following the drug's demonstration of potent inhibition of the PI3K pathway in the brain, paxalisib was taken into the clinic.



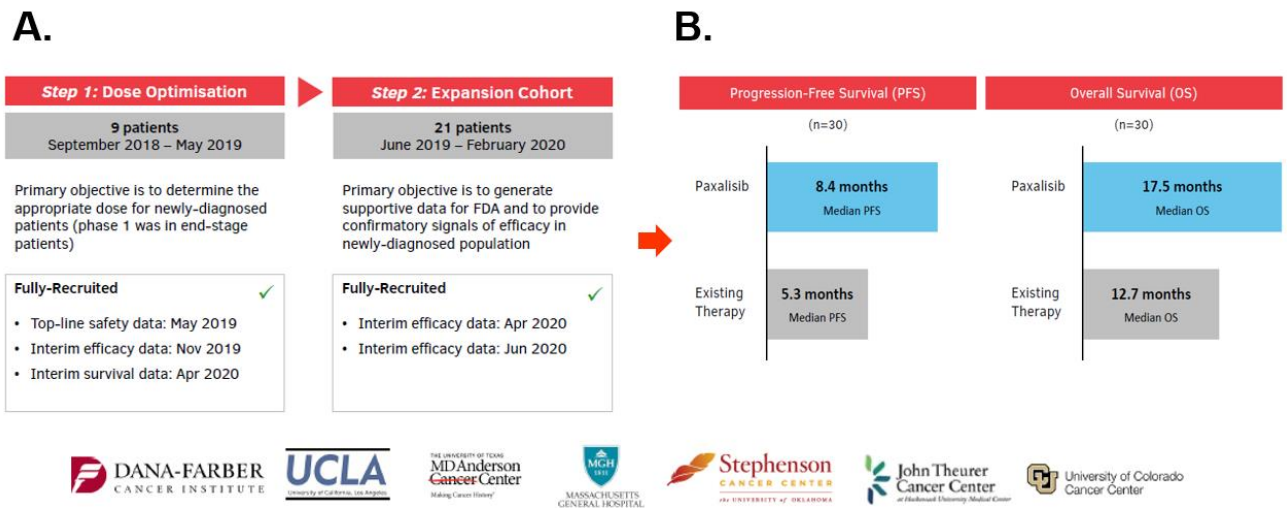
Source: Adapted from Salphati L et al., 2016.

[20] Ellingson BM et al., Clin Cancer Res. 2020; 26(13):3135-3144.

Clinical development – glioblastoma multiforme

Phase 1 dose-escalation study. A first-in-human, open-label, multi-center Phase 1 study (NCT01547546) was conducted previously by Genentech in patients with recurrent high-grade glioma.[21] A total of 47 heavily pre-treated patients (with mean 3 prior systemic therapies) were enrolled across eight successive cohorts (2-65 mg paxalisib). The dose-escalation study followed a 3 + 3 design with patients on a 1x oral daily schedule (in cycles of 28). 48% of the patients had received bevacizumab in the immediate prior line of therapy. Dosing escalation continued until the maximal tolerated dose (MTD) was exceeded; MTD was determined to be 45 mg/day in the recurrent setting. On safety, paxalisib was shown to be generally well tolerated at 45 mg daily, and AEs were consistent with the established PI3K/mTOR inhibitor class effects. Mucositis was the predominant dose-limiting toxicity (DLT). There were no SEAs related to paxalisib higher than Grade 3. Dose-limiting toxicities included: one case of Grade 2 bradycardia and Grade 3 myocardial ischemia (15mg), Grade 3 stomatitis (45mg); and two cases of Grade 3 mucosal inflammation (65 mg). Among the evaluable patients (two were non-evaluable), best overall response was: 19 (40%) stable disease; and 26 (55%) progressive disease. Paxalisib demonstrated linear and dose-proportional PK and a half-life of ~19 hours that was supportive of 1x daily dosing. Based upon the initial signals of clinical activity in the Phase 1, paxalisib was entered into a trial in newly diagnosed glioblastoma patients.

Exhibit 13. Ongoing Phase 2 study is in newly diagnosed GBM patients. The Phase 2 study (NCT03522298) is evaluating the safety, tolerability and clinical activity of paxalisib in patients with newly diagnosed GM with unmethylated MGMT promoter status following surgical resection and chemoradiotherapy. **(A)** The open-label, single-arm study was designed in two parts. Step 1 (dose-escalation, n=9) was conducted to determine the maximum tolerated dose (MTD), which came to 65 mg. Step 2 (expansion n=21) is being conducted to determine preliminary evidence of clinical activity in newly diagnosed patients. Recruitment was completed in February 2020 and interim results were last reported at SNO 2020. **(B)** For the entire study population, paxalisib treatment saw a median progression-free survival (PFS) of **8.4 months,** which compares favorably to historical **5.3 months** for standard of care therapy (TMZ) in a similar patient population. Median overall survival (mOS) on paxalisib was **17.5 months vs. 12.7 months** (historical) with existing therapy. Important to note, no evidence of pneumonitis, cardiac toxicity, GI perforation, infection, CNS toxicity, or significant hepatotoxicity were documented. Safety was again consistent with other PI3K/mTOR inhibitors and the prior study. Most common AEs were rash (71%, Grade 1-3), stomatitis (46%, Grades 1-3), hyperglycemia (33%, Grades 1-3), fatigue (58%, Grades 1-3), nausea (38%, Grades 1-3), and decreased appetite (46%, Grades 1-3). While most AEs were Grades 1-3, there was one Grade 4 case of decreased neutrophils. Overall, paxalisib appears to have clinical activity in the GBM setting. Although this is a single arm study, we believe the single agent activity seen to date has been encouraging and suggests superiority to soc in OS and PFS (historical benchmark TMZ). We expect the final data readout at SNO 2021 to remain consistent with previous demonstrations of activity and safety.



Source: Company reports.

Safety. Altogether, >150 patients have been treated with paxalisib worldwide to date. While the drug has demonstrated AEs consistent with its class, there have been no significant safety signals observed such as diarrhea/colitis, intestinal perforation, hyperglycemia, and hypertension.

[21] Wen PY et al., Clin Cancer Res. 2020; 26(8):1820-1828.

Exhibit 14. Summary of paxalisib regulatory status designations. Paxalisib has several regulatory designations by the FDA. These include Orphan Drug, Fast Track and Rare Pediatric Disease Designations.

	Glioblastoma *Most common and most aggressive adult brain cancer*	**DIPG** *Highly aggressive childhood brain cancer*
Orphan Designation	February 2018	August 2020
Fast Track Designation	August 2020	
Rare Pediatric Disease Designation	n/a	August 2020

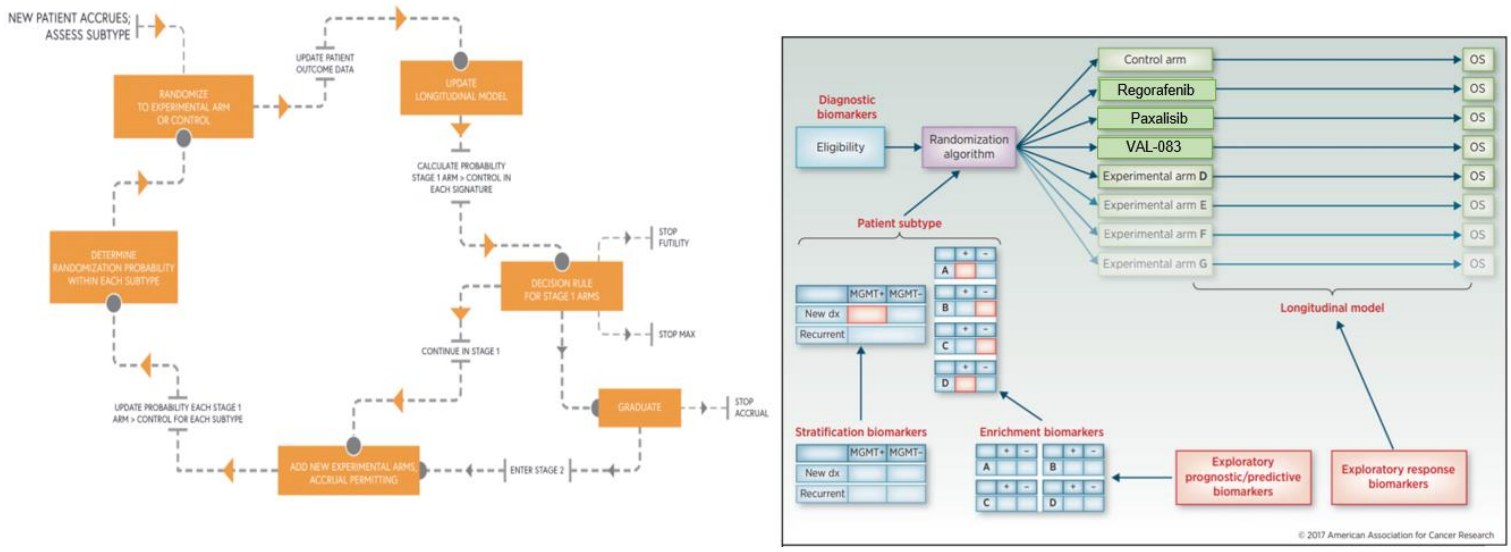
Source: Company reports.

Path to approval via AGILE GBM.[22] Traditional Phase 2 and Phase 3 trials have two arms with preset patient populations and preset sample sizes to address a single question, although more recent studies have begun to take a more adaptive approach, including attempting to match treatment arms with patient subtypes as defined by biomarkers. GBM AGILE (**G**lioblastoma **a**daptive, **g**lobal, **i**nnovative **l**earning **e**nvironment) is a departure from the standard clinical trial. It is a novel, two-stage, multi-arm platform and physician-led study with a personalized approach, tailored to accelerate the discovery of treatments for individual patients. More specifically, this randomized, adaptive, global, open-label Phase 2/3 trial is being conducted under one master protocol that allows for multiple investigational therapies or combinations of therapies from different biotech or pharmaceuticals partners to be evaluated simultaneously. The study is designed to investigate the therapies in both newly diagnosed and recurrent GBM patient populations vs. the one rolling control group (standard of care), with the goal of identifying effective therapies and the most promising biomarker-defined populations for those therapies. Important to note, there could potentially be more than one 'winner' here. The primary endpoint is overall survival; secondary endpoints include progression free survival and tumor response. The innovative study is driven by Global Coalition for Adaptive Research (GCAR), a nonprofit, international partnership and supported by the FDA and other regulatory agencies. Kazia's paxalisib joined the International GBM AGILE study (NCT03970447) in newly diagnosed and recurrent GBM patients in 2020. Most importantly, for Kazia, GBM AGILE provides paxalisib an expedited path to registration. We expect headline results from the study for Paxalisib in mid to late 2023, with potential for regulatory approval in 2024.

GBM AGILE is designed as a registration trial. Established by the collective work of over 130 oncologists, statisticians, pathologists, basic scientists, and other specialists (i.e., many leading experts in GBM) from more than 40 leading institutions, the trial is designed to take highly effective treatment arms rapidly through the trial to enable faster registration and regulatory review; and thus, accelerate availability of effective therapies. Importantly, for Kazia, the study is intended to serve as the pivotal study for paxalisib in multiple markets, including the US, EU, and China.

Exhibit 15. GBM AGILE is an adaptive multi-drug registrational study with strong FDA support. The primary endpoint is overall survival and experimental therapies can enter the trial at any time. The trial consists of two stages. **Stage 1** is a screening stage to evaluate many therapies (including combinations); it uses a sophisticated statistical approach called 'adaptive randomization' among the experimental arms within clinical and biomarker subtypes. Meaning, if one treatment outperforms another, a higher proportion of new enrollees will be assigned to that treatment arm. In addition, it readjusts its statistical power as it goes. Up to 150 patients can be recruited in this stage in a given cohort. Therapies that are sufficiently promising in the screening stage will move to a confirmatory stage with fixed randomization. Accordingly, **Stage 2** is designed to confirm the signal in a small cohort (n=50) of patients using fixed randomization versus control. Highly effective treatment arms have the potential to proceed rapidly through the trial, enabling faster registration, regulatory review, and ultimately adoption. So long as an experimental arm remains on the study, enrichment biomarkers hypothesized to be predictive of response to a specific treatment will be evaluated. Promising arms that do not meet the criteria for the confirmatory stage are able to exit the trial with data that can help refine biomarker hypotheses and enable go/no go decisions outside of the trial. That said, the study (i.e., paxalisib cohort) may even be able to conclude early if efficacy can be determined before 200 patients are enrolled. GBM AGILE is operational at 31 sites in US and Canada and more sites are expected to open in the EU and China in 2021.

[22] Alexander BM et al., Clin Cancer Res. 2018; 24(4):737-743.



Source: https://www.gcaresearch.org/gbm-agile/; Alexander BM et al., 2018.

How does the trial work? From the company standpoint, Kazia supplies the drug and provides support for the paxalisib arm of the study, which includes some expenses as well. However, the cost of participating in this trial with a master protocol and control is limited (~1/3 of a traditional P3 trial for Kazia) compared to a standard standalone trial run directly by the company. GCAR, in turn, oversees the operational aspects of the trial, which includes site activation and patient recruitment and enrollment.

Patient enrollment. All patients are expected to have histologically confirmed Grade IV GBM. For the newly diagnosed cohort, upon entry, patients undergo surgery to remove the tumor, which is followed by radiation therapy plus with temozolomide (i.e., the Stupp regimen). Primary endpoint is overall survival with paxalisib or TMZ. For the recurrent arm, patients will have to have evidence of recurrent disease or progression (i.e., two scans to confirm) as assessed by modified RANO criteria. The study will assess the difference in OS for paxalisib vs. lomustine in the recurrent cohort.

Paxalisib joined GBM AGILE in 2020. In October 2020, the company executed a definitive agreement with GCAR to introduce paxalisib into the ongoing GBM AGILE study. The first drug to enter the study was Bayer's regorafenib in 2019. For paxalisib, the first site in GBM AGILE to open occurred at the end of December 2020; and the first patient was subsequently recruited on January 7, 2021. The initial focus is on sites in the United States, which has more than 40 leading cancer hospitals participating. Paxalisib is expected to expand to patients in Canada, the EU, and China thereafter (in 2021), which should enable acceleration of study recruitment, in our view. The paxalisib arm will be led by Principal Investigators Dr. Ingo Mellinghoff, Chair of the Department of Neurology at Memorial Sloan Kettering Cancer Center and Dr. Eudocia Q Lee, Director of Clinical Research at the Center for Neuro-Oncology at Dana-Farber and Assistant Professor of Neurology at Harvard Medical School. Dr Timothy Cloughesy (Director of the Neuro-Oncology Program of the Brain Research Institute at UCLA) is the Principal Investigator for the overall study.

GBM AGILE has three active therapeutics arms to date. The trial has three drug candidates currently under evaluation in three separate cohorts in both newly diagnosed and recurrent GBM:

- Bayer's regorafenib, an oral, multi-kinase inhibitor (VEGR2-TIE2) that is currently approved for metastatic colorectal cancer, gastrointestinal stromal tumor (GIST) and hepatocellular carcinoma;
- Kazia's paxalisib;
- Kintara Therapeutics' (KTRA - Buy) VAL-083 (chemotherapy), a bi-functional DNA targeting agent. VAL-083 is approved in China in acute myeloid leukemia (AML).

Our takeaways on GBM AGILE. Although participation in GBM AGILE does limit Kazia's control over the study, overall, we believe that the platform study will help Kazia to efficiently generate clinically meaningful results, which, if positive, can enable the company to bring paxalisib quickly to market. If paxalisib continues to demonstrate similar levels of clinical activity as the ongoing Phase 2 study, we are optimistic for the drug's success in the pivotal GBM AGILE trial. Results from the paxalisib arm are expected around mid-2023.
Taken together, we believe, participation in GBM AGILE offers multiple key advantages for Kazia:

- **Speed –** With an existing infrastructure (31 active sites and counting) and experimental design set up by GCAR, multiple drugs can be evaluated in parallel against a master control, allowing for faster enrollment; with an 'adaptive design,' the study is set up to only recruit

the number of patients needed to reach an 'answer' (up to 200 on paxalisib); altogether, GBM AGILE offers faster therapeutic development in GBM;
- **KOLs** – access to leading world experts in GBM;
- **FDA endorsement** – positive data from GBM AGILE will be suitable for drug registration;
- **Cost -** GBM AGILE has received substantial grant funding, greatly reducing the cost for participating companies.

GBM plus ketogenic diet

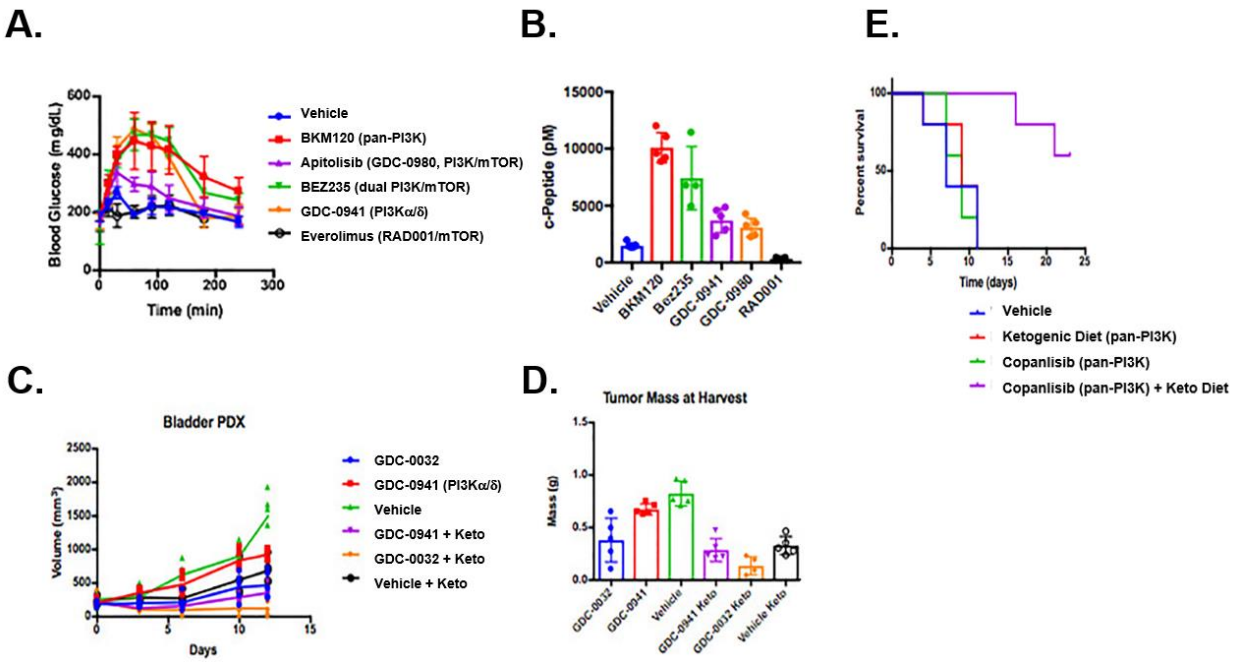
Disrupting insulin feedback with a ketogenic diet to increase PI3K inhibitor potency. On June 15, 2021, Kazia entered into a collaboration with Weill Medical College of Cornell University to investigate paxalisib in combination with ketogenesis (a ketogenic diet and metformin) in newly diagnosed or recurrent glioblastoma. What is ketogenesis? It is the process by which the body uses an alternative form of energy – where the body is fueled by metabolic fats and proteins instead of glucose (to produce ketones) – during states of starvation, as well as in response to a ketogenic diet (high-fat, adequate-protein, low-carbohydrate diet). Preclinical work by Professor Lewis Cantley of Weill Cornell, who discovered the PI3K pathway, suggests that ketogenesis may enhance the activity of PI3K inhibitors in certain tumor types such as glioblastoma.[23]

Does it make sense to combine a keto diet with paxalisib? In our view, yes. Variable clinical responses have been observed with pharmacologic inhibition of PI3K. Preclinical data suggest this phenomenon may be attributable to a possible inherent mechanism of resistance from insulin feedback induced by PI3K inhibition.[23] How? Under normal conditions, insulin is produced in the body in response to high levels of glucose. When cancers are treated with PI3K inhibitors, insulin signaling downstream of the pathway is also initially blocked. Insulin blockade prevents glucose uptake into the muscles and tissues, resulting in transient hyperglycemia (within a few hours of PI3K inhibitor administration). When this hyperglycemia becomes persistent in a subset of patients, it is managed pharmacologically. This side effect or complication of hyperglycemia, however, is typically transient because compensatory insulin is released to restore normal glucose homeostasis. The resulting insulin feedback is thought to be able to reactivate the PI3K/mTOR signaling axis in tumors. This, in turn, counters the anti-tumor effects of PI3K inhibitors, thereby limiting a drug's therapeutic potential. A Phase 2 combination study will begin by 2021 year-end to explore this hypothesis – whether the absence of glucose (by adding a ketogenic diet) to reduce insulin levels, would correspondingly improve PI3K drug efficacy.

Study design details. The Phase 2 study will be conducted at Weill Cornell Medical Center, led by Dr. Howard Fine, Director of the Brain Tumor Center at New York-Presbyterian Weill Cornell Medical Center. Professor Cantley will serve as a scientific advisor for the study. The trial will recruit patients in two cohorts (n=16 each). The first arm will contain patients with newly diagnosed GBM with unmethylated MGMT promotor status. The second arm will contain patients with recurrent disease that have progressed after taking standard-of-care therapy. Patients in both arms will be administered paxalisib and metformin, in combination with a ketogenic diet. The diet will be overseen by clinical dieticians to ensure compliance. If there are signals of efficacy in a given arm, that arm will be expanded to ~30 patients. The primary endpoint is PFS at six months. The study will also investigate a range of metabolic and PD biomarkers. Recruitment is expected to start by end of 2021.

Exhibit 16. Preclinical data suggests that a ketogenic diet in combination with paxalisib may significantly enhance the activity of paxalisib.[23] **(A)** When wild-type mice are treated with therapeutic doses of compounds targeting a variety of kinases in the insulin receptor/PI3K/mTOR pathway, many of the agents cause significant increases in blood glucose levels. The hyperglycemia resolves after a few hours without additional intervention. **(B)** For most of the agents, there is also an increase in the amount of insulin released in the serum. Shown, measurement of c-peptide by ELISA, which is clinically used as a surrogate for insulin. Adding a ketogenic diet to mice bearing tumors following PI3K inhibition improves drug efficacy **(C, D, E)**. (C, D reduction tumor mass and volume, respectively, in PDX bladder model; E – increased survival is seen in pancreatic tumor model). Combined, the data suggest that insulin feedback can be prevented using dietary or pharmaceutical approaches, which limits the release of glucose, thereby greatly enhancing the cytotoxicity of these agents. If these observations can be recapitulated in the clinic, it would suggest that ketogenesis can synergize with the activity of paxalisib in GBM, and potentially minimize certain side effects such as hyperglycemia.

[23] Hopkins BD et al., Nature. 2018 (7719); 560:499-503.



Source: Adapted from Hopkins BD et al., 2018.

Clinical development – brain metastases

Brain metastasis. CNS metastasis can be a frequent complication (especially) for certain tumor types. As with most primary brain tumors, brain metastasis carries a poor prognosis. Median survival ranges between 3 to 27 months after metastatic spread to the brain occurs.[24] Approximately 8% to 10% of patients with cancer will develop brain metastases, and up to 30% of patients with metastatic cancer will develop brain metastasis.[25] More than half of these patients will die within a few months after their diagnosis of intracranial metastasis.[25,26] Lung, melanoma and breast cancers are the most common histologies that metastasize to the brain. In addition, an estimated 50% of lung cancer, advanced breast and advanced melanoma patients will also develop brain metastasis.[27,28]

Current treatment protocol for brain mets. Effective treatments are limited. Notably, radiation therapy (RT) has been the mainstay in this setting, following surgery, but still offers limited survival benefit.[29] Many chemotherapy agents do not cross the blood-brain barrier; and, thus, are not effective in the treatment of brain metastases. Patients eventually also progress with chemotherapeutic agents that cross the BBB. Though some tyrosine kinase inhibitors have shown some benefit for patients harboring select mutations or rearrangements (e.g., EGFR, HER2), it does not reflect the majority of patients. Even in those instances, after initial tumor control, the cancers progress. While immunotherapy is rapidly become the standard of care in cancer indications such as metastatic lung cancer and melanoma, the majority of patients treated with immunotherapy progress in the CNS. As such, novel targets are needed.

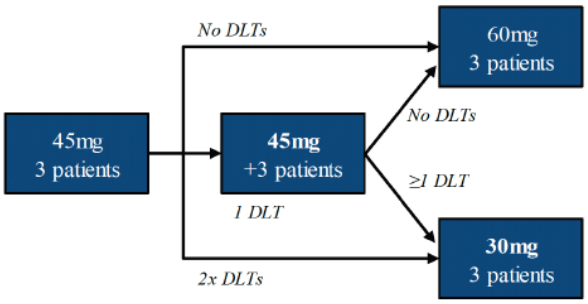
Beyond GBM. Paxalisib is being explored in multiple brain cancers, including brain metastases. Paxalisib is currently being evaluated in several investigator-sponsored trials (ISTs):

- Memorial Sloan Kettering Cancer Center - P1 study in PIK3CA-mutated solid tumor brain mets, in combination with radiotherapy (NCT04192981);
- Alliance for Clinical Trials in Oncology/National Cancer Institute - P2 study in genetically defined brain mets (NCT03994796);
- Dana Farber Cancer Institute - P2 study in HER2+ breast cancer brain metastases, in combination with Herceptin (NCT03765983).

Exhibit 17. Study design of a Phase 1 trial of concurrent paxalisib with RT in patients with brain metastases. Up to 30% of patients with metastatic cancer will develop brain metastases and/or leptomeningeal (membranes linings of the brain) metastases.[25] Radiation therapy (RT) is the standard treatment. While effective resistance to RT will ultimately occur and tumor resistance to RT often results from hyperactivation of the PI3K pathway. To evaluate paxalisib and RT combination treatment to potentially improve CNS disease control, an open-label, prospective

[24] Brastianos PK et al., J Natl Compr Canc Netw 2013;11:1153-1164.
[25] Brastianos PK et al., Cancer Discov. 2015; 5(11):1164-1177.
[26] Cagney DN et al., Neuro Oncol 2017; 19(11):1511-1521.
[27] Dagogo-Jack I et al., Trends Cancer. 2016; 2(7):332-337.
[28] Dagogo-Jack I et al., Pharmacol Ther.2017; 170: 64-72.
[29] Gasper LE et al., J Neurooncol, 2010. 96(1): p. 17-32.33.

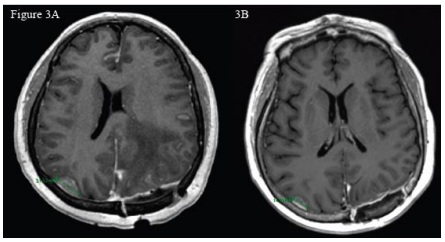
Phase 1 dose-escalation study (N= up to 24) was initiated at Memorial Sloan Kettering in patients with brain or leptomeningeal metastases. The study is expected to enroll patients with metastatic solid tumors harboring PI3K pathway mutations (specifically, PIK3CA mutation). The primary aim is to assess the toxicity and safety of paxalisib in combination with RT (30Gy in 10 fractions) to the brain. Secondary endpoints include local control per Response Assessment in Neuro-Oncology, intracranial progression-free survival and overall survival. The starting dose is 45 mg 1x daily, and three doses are being explored: 45 mg, 60 mg, 75 mg, with potential de-escalation to 30 mg to determine MTD in combination with radiation therapy to the brain. Once the MTD is reached, an expansion cohort (n=12) will be treated. Exploratory biomarkers from pre- and post-treatment cerebrospinal fluid will be investigated as well (circulating tumor cells, mutated allelic burden in cell-free DNA, cytokines, RNA and protein analysis of the cellular component).



Source: Yang TJ et al., AACR 2020.

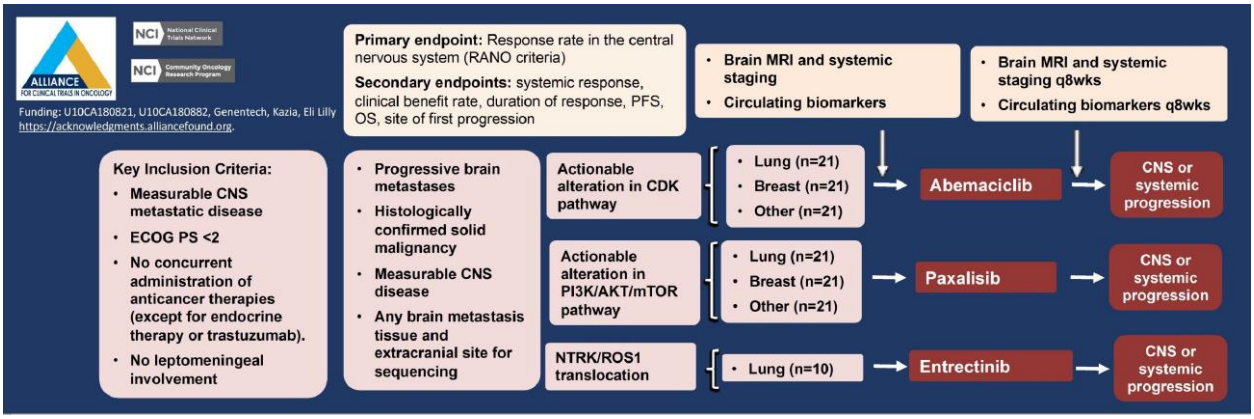
Rationale for combining paxalisib with RT. PI3K inhibitors on their own elicit cytotoxic activity. However, PI3K inhibitors are also believed to enhance the effects of RT treatment, which includes radiation-induced DNA damage, G2/M arrest, and apoptosis. For example, RT can induce phosphorylation of Akt, which together with direct PI3K-Akt inhibition by paxalisib can cause downregulation of pro-survival pathways; thus, rendering a synergistic effect. In addition, paxalisib can cause significant decrease in glycolysis (via mTOR inhibition), which can impact a cell's ability to undergo efficient DNA repair, thereby also ultimately causing DNA damage, leading to further tumor killing.

Exhibit 18. Robust response observed in one brain mets patient. Since the investigator-sponsored trial initiated, one patient has successfully completed therapy without experiencing any DLTs at the 45 mg dose. AEs experienced were nausea (Grade 1), diarrhea (Grade 1), respiratory infection (Grade 2), and fatigue (Grade 2). However, none were believed to be attributable to paxalisib. Shown: MRI brain at enrollment (3A) and one month after RT (3B).



Source: Yang TJ et al., AACR 2020.

Exhibit 19. The P2 Alliance trial is looking at genetic testing to guide brain metastasis treatment. Some gene expression signatures are associated with metastasis to the brain; and mutations in NTRK, ROS1, CDK or PI3K are among those that have been frequently found to be altered.[25] As such, genetic testing may facilitate tailoring treatment for each mutation. Further, medications that target these genes such as paxalisib for PI3K/mTOR may stop the growth of tumor cells by blocking some of the enzymes needed for cell growth. The Alliance trial is an open-label, multi-center and multi-arm genomically guided clinical study that will explore targeted agents in matched patients with brain metastases harboring alterations associated with sensitivity to three inhibitors: abemaciclib (CDK inhibitor), paxalisib (PI3K/mTOR inhibitor) and entrectinib (NTRK/ROS1 inhibitor). Patients with new, recurrent or progressive brain metastases with tumors ≥1cm will be eligible for the trial. Each of the CDK and PI3K inhibitor and tumor cohorts (breast, lung and other) will have 21 evaluated patients each, while the NTRK/ROS1 cohort (lung) will have 10 patients assigned to the cohort for a total of 136 evaluable patients. The primary endpoint is objective response rate as assessed by RANO (Response Assessment in Neuro-Oncology) criteria. The study is currently accruing patients.



Source: Brastianos PK et al., ASCO 2020.

Phase 2 study in HER2-Positive Breast Cancer. Although breast cancer accounts for the most common malignancy worldwide and represents the second most frequent primary tumor causing brain metastases, management of affected patients remains a challenge. Upregulation of the PI3K pathway occurs in up to 70% of patients with breast cancer brain metastases (BCBM).[30] Accordingly, inhibition of PI3K is a particularly appealing strategy for the treatment of BCBM. In preclinical models, paxalisib has demonstrated inhibition of tumor growth.[31] Further, the data suggest that PI3K/mTOR blockade may be able to overcome resistance mechanisms (to HER2-directed treatment). Following these findings, a Phase 2 study (N=47) was initiated at the DFCI to evaluate paxalisib in combination with Herceptin in patients with HER2+ breast cancer mets patients. The primary endpoint is ORR.

Clinical development – diffuse intrinsic pontine glioma (DIPG)

Paxalisib's appeal – other opportunities in brain cancer settings provide upside. In addition to participating in multiple investigator-sponsored studies for brain metastases and GBM, paxalisib is also being evaluated in diffuse intrinsic pontine glioma (DIPG). (See Exhibit 11) DIPG is an invasive, fatal childhood brain tumor. Approximately 300 children in the US are diagnosed with DIPG each year; and children diagnosed with DIPG typically have less than 10% 2-year survival rate. Like GBM, these aggressive tumors are infiltrative and cannot be fully removed surgically. Radiation (RT) is the standard treatment. While an initial IST with paxalisib plus RT (conducted at St. Jude's, NCT03696355) has not shown clear signs of clinical efficacy in DIPG, we believe the upcoming platform DIPG study (PNOC022, NCT05009992) in collaboration with PNOC that is about to initiate (by YE21) could be more promising. Kazia has entered into a collaboration with the Pacific Pediatric Neuro-Oncology Consortium (PNOC), an international non-profit consortium of clinical sites to evaluate different combinations of promising drug candidates in DIPG. Drugs being evaluated in this study include:

- **Chimerix's (CMRX - Buy) ONC201** – an oral small molecule that targets two proteins (dopamine receptor D2 and ClpP, mitochondrial enzyme). The drug is currently being evaluated as a monotherapy in a registration-directed cohort (N=50) of patients >2 years of age with recurrent diffuse midline glioma harboring the H3 K27M mutation;
- **Novartis' Farydak (panobinostat)** – HDAC inhibitor that is currently approved for multiple myeloma;
- **Kazia's paxalisib.**

MODELING ASSUMPTIONS

Modeling Assumptions for Glioblastoma Multiforme (GBM)

1. We assume commercialization of paxalisib in 1L GBM in the US, EU, and in China beginning in 2024.
2. We assume 65% of GBM patients are MGMT promoter unmethylated.
3. We assume about ~7K, ~15K and ~35K GBM patients are eligible for treatment with paxalisib in the US, EU, and China, respectively.
4. We assume an annual initial cost of treatment of $186K (A$255K) in the US. Given the paucity of newly approved therapeutics in glioblastoma, we look to the costs of checkpoint blockades, Piqray (novel PI3K pathway inhibitor) and the Optune medical device. Piqray was approved in 2019 for HR+/HER2- breast cancer patients and was given a monthly list price of $15,500 ($186K annual). Similarly, anti-PD1s, Opdivo and Keytruda, are currently priced around $14K-$15K/month ($168K -$180K). Finally, the Optune device costs about $21k/month ($252K annual). For the EU market, we assume a 35% discount to the US price; and we assume a 49% discount for the China market.
5. We assume a 2% annual price increase for paxalisib.

[30] Adamo B et al., Breast Cancer Res. 2011; 13(6):R125.
[31] Ippen FP et al., Clin Cancer Res. 2019; 25(11):3374-3383.

6. We use assume a 15% royalty revenue to Kazia from an EU commercial partner and 13% royalty revenue from Simcere for the China market.
7. We apply a 70% risk adjustment based on clinical risk associated with therapeutics for glioblastoma.

Exhibit 20. Market Model for GBM (US, EU, China).

Paxalisib - Glioblastoma (US)	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E
Newly diagnosed GBM patients	10,746	10,854	10,962	11,072	11,183	11,295	11,408	11,522	11,637	11,753	11,871
% growth	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*	*1%*
% Unmethylated GBM	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*	*65%*
Eligible patients	6,985	7,055	7,126	7,197	7,269	7,341	7,415	7,489	7,564	7,640	7,716
Market Penetration				*3.0%*	*5.0%*	*7.0%*	*9.0%*	*15.0%*	*20.0%*	*22.0%*	*37.5%*
Total Patients Treated				216	363	514	667	1,123	1,513	1,681	2,893
Cost of Treatment				$255,000	$260,100	$265,302	$270,608	$276,020	$281,541	$287,171	$292,915
Increase in Cost				*2%*	*2%*	*2%*	*2%*	*2%*	*2%*	*2%*	*2%*
Total revenue ('000)				$55,056	$94,531	$136,340	$180,588	$310,069	$425,911	$482,650	$847,545
Risk adjustment				*70%*	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*
Total Revenue AUD ('000)				**$13,865**	**$25,523**	**$36,812**	**$48,759**	**$83,719**	**$114,996**	**$130,316**	**$228,837**
Paxalisib - Glioblastoma (EU)	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**
Total Partner Revenue AUD ('000)				**$18,742**	**$27,032**	**$43,761**	**$61,477**	**$67,555**	**$95,694**	**$116,508**	**$184,656**
Total Kazia Royalty Revenue AUD ('000)	*15%*			**$2,530**	**$3,649**	**$5,908**	**$8,299**	**$9,120**	**$12,919**	**$15,729**	**$24,929**
Paxalisib - Glioblastoma (China)	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**
Total Simcere Revenue AUD ('000)				**$1,962**	**$33,696**	**$76,369**	**$107,285**	**$117,893**	**$166,999**	**$172,042**	**$185,294**
Total Kazia Royalty Revenue AUD ('000)	*13%*			**$230**	**$3,942**	**$8,935**	**$12,552**	**$13,794**	**$19,539**	**$20,129**	**$21,679**

Source: Maxim Estimates

Modeling Assumptions for Brain metastases

1. We assume market entry for paxalisib brain metastases (from lung cancer: NSCLC), metastatic melanoma and breast cancer in 2025 in the US and 2026 in the EU and China markets.
2. We assume 94K in the US, 132K in the EU, and 293K in China are eligible for paxalisib treatment.
3. We assume an initial monthly cost of treatment of $16K (A$22K) in the US, based on our annualized cost of $186K for GBM. We assume a 65% discount price for the EU market, and a 49% discount for the China market.
4. We assume a 2% annual price increase for paxalisib
5. We use assume a 15% royalty revenue to Kazia from an EU commercial partner and 13% royalty revenue from Simcere for the China market.
6. We apply a 70% risk adjustment based on clinical risk associated with therapeutics for secondary brain tumors.

Exhibit 21. Market Model for brain metastases (US, EU, China).

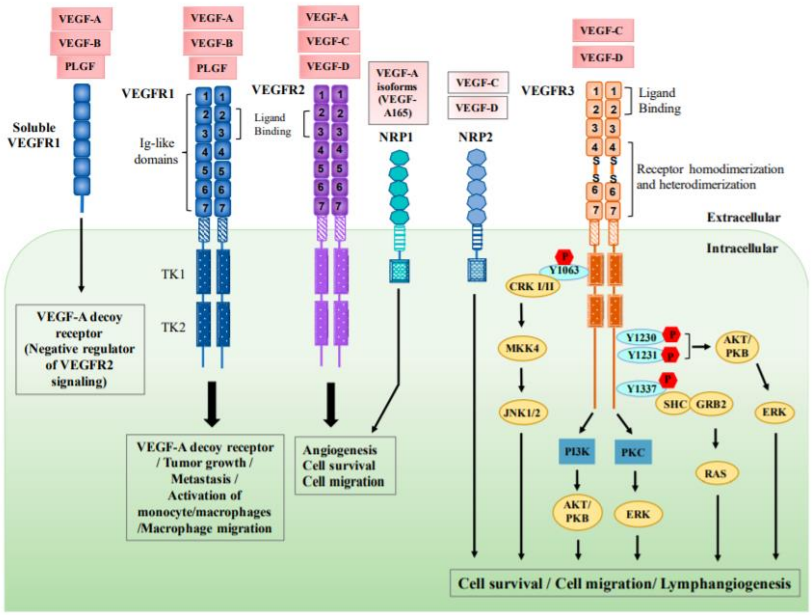
Paxalisib - Brain mets (US)	2021E	2022E	2023E	2024E	2025E	2026E	2027E	2028E	2029E	2030E	2031E
US population	333,482,500	335,983,619	338,503,496	341,042,272	343,600,089	346,177,090	348,773,418	351,389,219	354,024,638	356,679,823	359,354,921
Non-small cell lung cancer incidence (NSCLC)	195,738	197,695	199,672	201,669	203,686	205,723	207,780	209,858	211,956	214,076	216,217
NSCLC advanced / metastatic (*80%*)	156,590	158,156	159,738	161,335	162,949	164,578	166,224	167,886	169,565	171,261	172,973
Brain mets (*50%*)	78,295	79,078	79,869	80,668	81,474	82,289	83,112	83,943	84,782	85,630	86,487
Breast cancer incidence (invasive)	281,550	284,366	287,209	290,081	292,982	295,912	298,871	301,860	304,878	307,927	311,006
Breast cancer advanced / metastatic	56,310	56,873	57,442	58,016	58,596	59,182	59,774	60,372	60,976	61,585	62,201
Brain mets (*25%*)	14,078	14,218	14,360	14,504	14,649	14,796	14,944	15,093	15,244	15,396	15,550
Melanoma incidence	106,110	107,171	108,243	109,325	110,418	111,523	112,638	113,764	114,902	116,051	117,211
Melanoma advanced / metastatic	8,489	8,574	8,659	8,746	8,833	8,922	9,011	9,101	9,192	9,284	9,377
Brain mets (*20%*)	1,698	1,715	1,732	1,749	1,767	1,784	1,802	1,820	1,838	1,857	1,875
Eligible patients	94,070	95,011	95,961	96,921	97,890	98,869	99,858	100,856	101,865	102,883	103,912
Market Penetration					*0.5%*	*1.2%*	*1.5%*	*2.0%*	*5.0%*	*7.0%*	*8.0%*
Total Patients Treated					489	1,186	1,498	2,017	5,093	7,202	8,313
Duration of therapy (cycles)					*8*	*8*	*8*	*8*	*8*	*8*	*8*
Cost of Treatment (monthly)					$22,000	$22,440	$22,889	$23,347	$23,814	$24,290	$24,776
Increase in Cost					*2%*	*2%*	*2%*	*2%*	*2%*	*2%*	*2%*
Total revenue AUD ('000)					$86,143	$212,988	$274,275	$376,744	$970,304	$1,399,449	$1,647,672
Risk adjustment					*70%*	*70%*	*70%*	*70%*	*70%*	*70%*	*70%*
Total Revenue AUD ('000)					**$23,259**	**$57,507**	**$74,054**	**$101,721**	**$261,982**	**$377,851**	**$444,871**
Paxalisib - Brain mets (EU)	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**
Total Partner Revenue AUD ('000)						**$57,726**	**$74,189**	**$101,704**	**$156,852**	**$268,780**	**$276,349**
Total Kazia Royalty Revenue AUD ('000)	*15%*					**$7,793**	**$10,016**	**$13,730**	**$21,175**	**$36,285**	**$37,307**
Paxalisib - Brain mets (China)	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**
Total Partner Revenue AUD ('000)						**$88,526**	**$113,733**	**$155,858**	**$240,285**	**$370,445**	**$423,048**
Total Kazia Royalty Revenue AUD ('000)	*13%*					**$10,358**	**$13,307**	**$18,235**	**$28,113**	**$43,342**	**$49,497**

Source: Maxim Estimates

Targeting Lymphangiogenesis with EVT801

One of the hallmarks of cancer is tumor angiogenesis (the formation of new blood vessels from pre-existing vasculature).[32] That is, for tumor growth to occur and metastasize, it requires blood vessels for nutrients and oxygen. This process of new vasculature formation is mediated by the vascular endothelial growth factor (VEGF) family of proteins.[33] VEGF is expressed in multiple tumor types and is also upregulated in the tumor microenvironment. Upregulation of VEGF has been shown to be driven via oncogene expression, a variety of growth factors as well as hypoxia.[34] Following the recognition of VEGF as a key regulator of angiogenesis, VEGF ligands and receptors of the VEGF signaling axis have been a common target for drug development, the most prominent of which is Genentech's Avastin (bevacizumab, which was the first drug approved to target this pathway).

Exhibit 22. VEGF family. Physiologic angiogenesis is important in wound healing, ovulation, and pregnancy but is also implicated in pathological conditions such as cancer.[35] The VEGF family plays an integral role in angiogenesis.[2] Six secreted glycoproteins make up the VEGF family of ligands: VEGF-A (VEGF), VEGF-B, VEGF-C, VEGF-D, VEGF-E, and placental growth factor (PGF). VEGF exerts its activity through binding to several transmembrane receptors: three VEGF tyrosine kinase receptors (VEGFR1, VEGFR2, and VEGFR3) and two non-enzymatic receptors (neuropilin-1 and -2) that which act as coreceptors for specific VEGF isoforms. Binding of the VEGFR tyrosine kinases results in dimerization, receptor autophosphorylation, and activation of downstream signal transduction pathways, leading to endothelial cell proliferation and blood vessel formation. While angiogenesis is primarily transduced through VEGFR2, lymphangiogenesis (formation of lymphatic vessels) signals are transduced by VEGFC/D via VEGFR3.[36]



Source: Hsu MC et al., 2019.

Exhibit 23. VEGF pathway is a validated therapeutic target. Blockade of angiogenesis has been a major target of cancer therapeutics, some of which have become blockbuster drugs. Avastin, for example, the first approved (2004) anti-angiogenic, which generated $7B at its peak still generated $5.3B in 2020, despite the introduction of biosimilars. These approved angiogenic tyrosine kinase inhibitors (TKIs) have differential binding capacities to angiogenic kinases. While bevacizumab binds and inhibits VEGFA alone, the other approved therapeutics are multi-kinase inhibitors (e.g., sorafenib, sunitinib, pazopanib). Most of these therapeutics are approved in multiple indications and represent a standard component of cancer treatment.

[32] Bergers G & Benjamin LE. Nat Rev Cancer. 2003;3(6):401–410.
[33] Nilsson M & Heymach JV. J Thorac Oncol. 2006; 8:768-770.
[34] Carmeliet P. Oncology. 2005; 69 Suppl 3:4-10.
[35] Hicklin DJ & Ellis LM. J Clin Oncol. 2005; 23(5):1011-1027.
[36] Stacker SA et al., Nat Rev Cancer. 2014;14 (3):159-172.

Product	Company	Target	Indications	Annual Sales (US$)*
AVASTIN bevacizumab	Genentech	VEGF-A	• Colorectal cancer • Lung cancer • Breast cancer • Other cancers	$7 billion
Nexavar (sorafenib) tablets	BAYER	VEGFR PDGFR RAF kinases	• Hepatocellular carcinoma • Renal call carcinoma • Thyroid cancer	$1 billion
SUTENT sunitinib malate	Pfizer	VEGFR PDGFR	• Renal cell carcinoma • Gasto-intestinal stromal tumor	$750 million
Votrient pazopanib tablets (200 mg)	NOVARTIS	VEGFR PDGFR c-Kit FGFR	• Renal cell carcinoma • Soft tissue sarcoma	$1 billion
Inlyta axitinib	Pfizer	VEGFR c-Kit PDGFR	• Renal cell carcinoma	$400 million

*Approximate, based on company filings and marked data

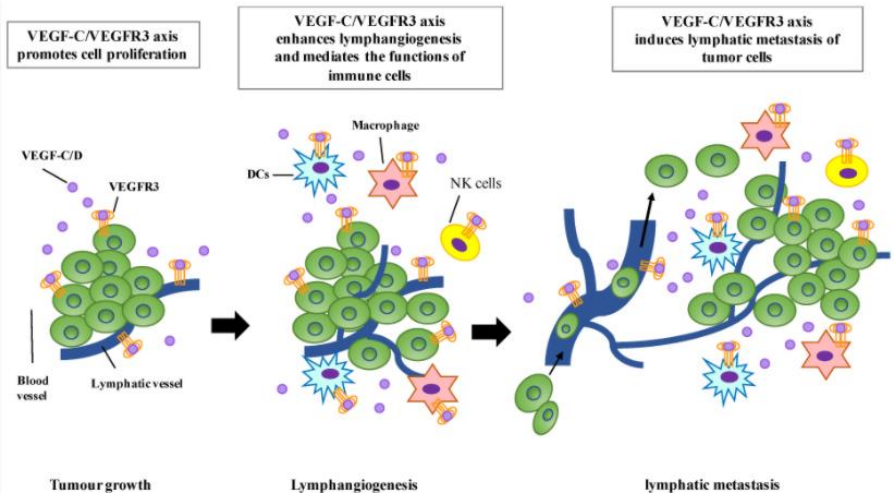
Source: Modified company reports.

'Choking off the blood supply' may not be enough. By preventing the formation of new blood vessels, tumors can be starved of nutrients, growth factors and oxygen, thus blocking tumor growth and dissemination of tumor cells to distal sites. Following this recognition, VEGF inhibitors have since become standard treatment across all lines of therapy in a range of tumor types and have been one of the most successful approaches to the treatment of cancer. In some indications, such as metastatic renal cell carcinoma (mRCC), VEGF(R)s have entirely changed the therapeutic landscape. In 1L alone, there are at least three approved agents: sunitinib, pazopanib and bevacizumab + interferon-alpha. However, even though VEGF(R) inhibitors are widely used, they have their limitations. For one, their use comes at the expense of chronic side effects.[37] Among the spectrum of toxicities (albeit mostly manageable) associated with agents that target VEGF are: asymptomatic proteinuria, cardiovascular AEs (such as hypertension, thromboembolic or bleeding complications, myocardial ischemia, prolongation of the corrected QT interval), fatigue, gastrointestinal perforations and transaminase elevations (and sometimes hepatotoxicity). Secondly, resistance can occur owing to escape mechanisms.[38] Although antiangiogenic drugs starve the growing tumor of nutrients, they can also cause hypoxia around the tumor, which is believed to generate resistance to treatment.

Targeting lymphangiogenesis may potentially avoid the problem of resistance. The remodeling of existing lymphatics is also thought to be an important step in tumor progression and cancer metastasis.[36] Targeting lymphangiogenesis achieves the same objectives as targeting angiogenesis, given that the lymphatic system is also a common route of metastases. However, inhibiting lymphangiogenesis may avoid the problem of resistance that results from hypoxia. As with angiogenesis, VEGF and its receptors play a pivotal role in pathologic lymphangiogenesis. Specifically, transduction signals and lymphatic metastasis occur through VEGFC/D via VEGF receptor 3 (VEGFR3).[36]

Exhibit 24. The VEGF-C/VEGFR3 axis promotes tumor growth via lymphangiogenesis and lymphatic metastasis of tumor cells.[36] Although VEGFR3 may also be expressed on tumor-associated blood vessels (and regulates sprouting angiogenesis and blood vessel growth), in healthy adults, VEGFR3 is primarily limited to the lymphatic endothelium and facilitates outgrowth of lymphatic vessels through binding of VEGF-C and VEGF-D. In concert, VEGF-C/VEGFR3 signaling can mediate the functions of immune cells such dendritic cells (DCs), macrophages, and natural killer (NK) cells.[39]

[37] Schmidinger M. EJC Suppl. 2013; 11(2):172-1919.
[38] Itatani Y et al., Int J Mol Sci. 2018; 19(4):1232.
[39] Hsu MC et al., Cells. 2019; 8(3):270.

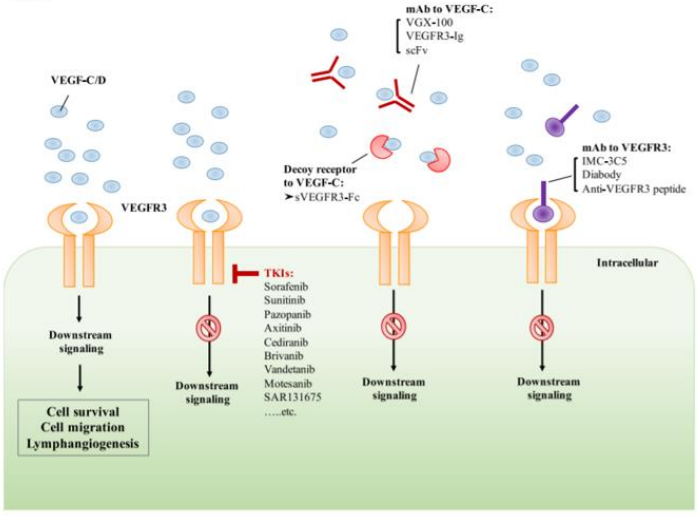


Source: Hsu MC et al., 2019.

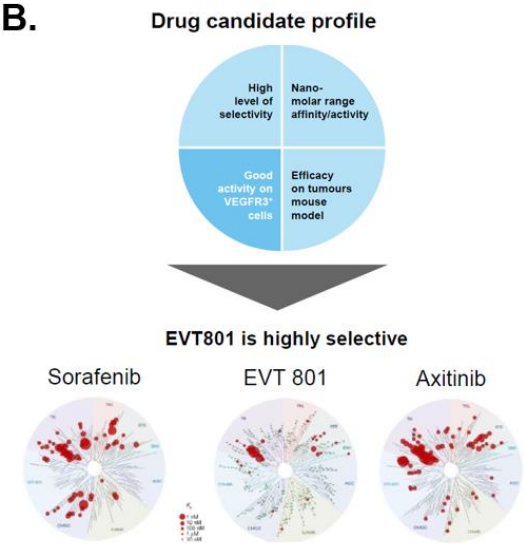
Broadening the pipeline with EVT801. On April 19, 2021, Kazia announced an in-license deal whereby the company had acquired the worldwide rights to a new VEGFR inhibitor from Evotec, a German-based drug discovery and development company. Originally discovered by Sanofi (SNY- NR), EVT801 was subsequently developed by Evotec in collaboration with Sanofi. EVT801 is a small molecule inhibitor of VEGFR3. While the drug's primary activity is the inhibition lymphangiogenesis, EVT801 is believed to also modulate the activity of the immune system, potentially enabling synergistic combination with immuno-oncology therapies.

Exhibit 25. EVT801 is a selective VEGFR3 inhibitor drug candidate. Few have targeted VEGFR3 specifically to inhibit lymphangiogenesis. **(A)** While several commercial drugs do inhibit VEGFR3 (such as sorafenib), they are multi-tyrosine kinase inhibitors; and thus, have other targets, which can often lead to significant side effects. **(B)** In contrast, Kazia's drug, EVT801 is a narrow spectrum inhibitor of the VEGFR3 tyrosine kinase with residual activity against VEGFR2 and TAK1. Given that EVT801 has a high degree of specificity for VEGFR3 (versus other signaling proteins in the VEGF pathway), it should exhibit a differential activity profile in the clinic from others in its class, including minimize toxicity. An improved safety profile would suggest that the drug may allow for longer duration of treatment and enable combinations with other therapeutics such as checkpoints, in our view. **(C)** In addition, given that VEGFR3 is expressed in multiple tumor types, EVT801 could potentially be used in such settings.

A.



B.



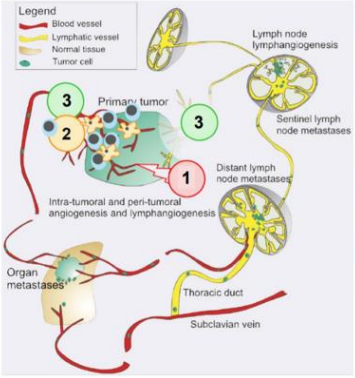
C.

VEGFR3 expression in tumor and microenvironment (%)

Indication	HCC	HNSCC	NSCLC	Lung AC	Kaposi	Renal	Colon
VEGFR3 expression in TME	30%-100%	40%	100%	100%	100%	94%	30%

Source: Hsu MC et al., 2019; Modified Evotec Company Reports Abstract #3970.

Exhibit 26. EVT801's novel mechanism of action. EVT801 is believed to control tumor growth through three means: **(1)** by inhibiting VEGFR3-expressing tumor cells; **(2)** by stimulating increase in infiltration of effector T cells and reduction of immunosuppressive myeloid cells; and **(3)** by stabilizing the tumor vasculature and reducing hypoxia. Combined, EVT801 is believed to not only be able to starve tumor cells of vital nutrients and reduce metastasis, but it may also be able to alter the activity within the tumor microenvironment. The latter, in turn, may enhance the activity of immuno-oncology therapies.

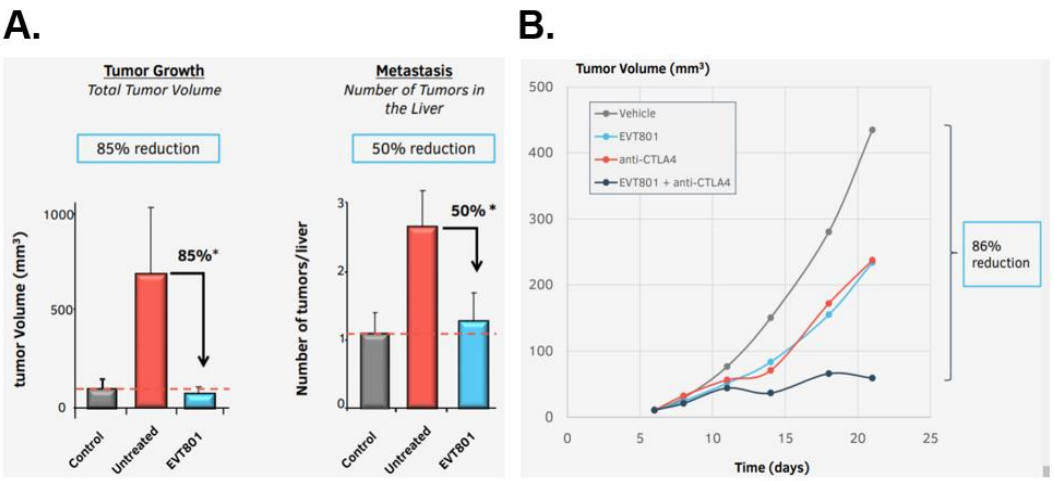


EVT801 mode of action offers efficacy advantages over other therapies

Drugs	Anti angiogenesis	Immune compartment
Pan-TKI inhibitor	Transient blood vessel normalization • Hypoxia • Necrosis	• Inhibition of T-cell proliferation
Avastin (VEGFR2/VEGFA interaction)	Transient blood vessel normalization • Hypoxia • Necrosis	• ND
IMC-3C5 (VEGFR3/VEGFC interaction)	• ND	• ND
EVT801	Sustained blood vessel normalization • **No increase of hypoxia** • **No increase of Necrosis**	• No negative impact on T-cell proliferation

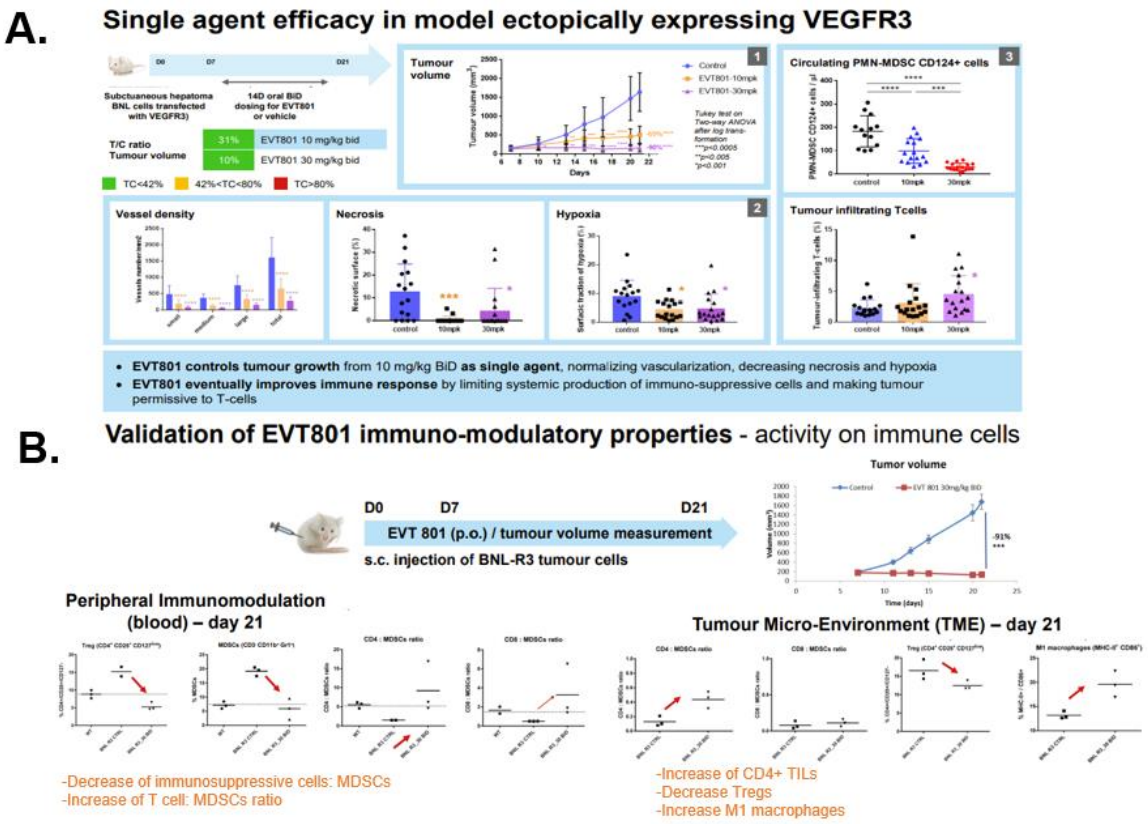
Source: Kazia Therapeutics Limited Company Reports; Evotec Company Reports Abstract #2132.

Exhibit 27. EVT801 is active in vivo. In preclinical models, EVT801 has demonstrated antitumor activity across a variety of tumor types, including synergy with immune-oncology agents. (Shown) **(A)** For example in a mouse hepatocellular model, treatment with EVT801 showed significant tumor growth reduction both as monotherapy and **(B)** in combination with anti-CTLA-4. Treatment with EVT801 as a single agent also demonstrates decrease in liver metastasis **(A)**.



Source: Company reports.

Exhibit 28. Inhibition of VEGFR3 leads to reduction of tumor growth by acting on the tumor microenvironment (TME). (Shown) **(A)** In a mouse model ectopically expressing VEGFR3 (BNL hepatoma cells transfected with VEGFR3), EVT801 administration **(1)** decreases tumor development, which occurs **(2)** without inducing an increase in hypoxia. **(B)** In the same model, EVT801 demonstrates the ability to change the balance of immune cells within the tumor microenvironment. More specifically, EVT801 demonstrates strong tumor-associated immunosuppression, manifested by decreased MDSCs (Myeloid Derived Suppressor Cells) and CD4- regulatory T cells and increased macrophages with a M1 phenotype inside the tumor. As a consequence, the Tcell:MDSC ratio increases in the TME and in the peripheral blood. (Not shown) In addition, in preclinical studies, EVT801 in combination with checkpoints such as PD1 mAb shows superior activity to single agent treatment. EVT801 treatment also increases CD8+ T-cells infiltration inside the tumor. Taken together, the results suggest a novel anti-angiogenic therapeutic for cancer immunotherapy that has the potential to improve response to an immune checkpoint (and thus extend their use) by sensitizing the tumors to current IO therapies, in our view.



Source: Evotec Company Reports: Modified Abstract#2132; Abstract #3970.

Next steps. On September 2, 2021, Kazia announced that the French regulatory agency, L'Agence Nationale de Sécurité du Médicament et des Produits de Santé (ANSM), had approved the initiation of a Phase 1 study for EVT801 in patients with advanced solid tumors. Two leading cancer hospitals in France will serve as sites for the study: Oncopole in Toulouse and Centre Léon Bérard in Lyon. Initial indications to be explored include renal cell carcinoma (kidney cancer), hepatocellular carcinoma (liver cancer), and soft tissue sarcoma. The Phase 1 study is expected to begin recruitment by end of 2021.

We do not currently ascribe value to the EVT801 program, which we view as potential upside.

Partnerships / Licenses

Out-licensing deals

Cantrixil (Novogen legacy asset)

Oasmia Pharmaceutical AB (OASM.ST - Not Rated). Following the conclusion of the open-label Phase 1 study of Cantrixil in December 2020, which was conducted at sites in the US and Australia, Kazia found a partner with an existing commercial structure and know-how to advance the legacy asset developed by its predecessor, Novogen Limited. On March 1, 2021, Kazia reported out-licensing Cantrixil (ovarian cancer drug) to the Swedish, oncology-focused specialty pharmaceutical company drug company, Oasmia. Oasmia already has one marketed ovarian cancer product, Apaelea, in the EU market. Oasmia will assume exclusive global rights to develop and commercialize Cantrixil for all indications (with a focus on ovarian cancer). Under the terms of the agreement, Kazia received an upfront payment of $4M, and is eligible for milestone payments of up to $42M, and double-digit royalties on commercial sales. Cantrixil is expected to enter a Phase 2 study in 2022.

Paxalisib

Simcere Pharmaceutical Group Ltd (HKSE: 2096 - Not Rated). On March 29, 2021, Kazia announced that the company had entered into a license agreement with Simcere to develop and commercialize paxalisib for Greater China (specifically Mainland China, Hong Kong, Taiwan and Macau). Kazia received an upfront payment of $11M: $7M cash and $4M equity investment (at ~20% premium to trading at time of transaction). The company is eligible to receive up to $281M in potential milestone payments for glioblastoma, as well as further milestones for indications beyond GBM. Kazia is also eligible to receive royalties on commercial sales in the mid-teens for paxalisib.

- **Simcere.** As one of China's leading pharmaceutical companies, Simcere has over 40 marketed products in addition to an extensive development pipeline. The company generated ~$329M or (CN¥2.12B) in revenue in 1H21. Simcere boasts partnerships with numerous companies, both biotech and pharma, including Bristol Myers Squibb (BMY - NR) and G1 Therapeutics (GTHX - NR). Simcere's key areas of focus are oncology, diseases of the CNS, and autoimmune disease.
- **GBM AGILE.** Although Simcere is responsible for all clinical studies and regulatory steps associated with the Greater China territories, Kazia will continue to drive forward the Phase 3 GBM AGILE pivotal trial as planned, including study sites in China. As such, data from the GBM AGILE study is likely to meet regulatory requirements for China; and Kazia will work closely with Simcere to secure regulatory approval in China. Note, GBM AGILE is expected to launch (recruitment) in China by the end of 2021.

VALUATION

We model commercialization of paxalisib for 1L GBM in the US, EU and China markets in 2024; we model paxalisib in brain metastases in the US in 2025 and EU and China in 2026. A risk adjustment of 70% is factored in based on clinical trial risk. A 30% discount is applied to the free cash flow, discounted EPS, and sum-of-the-parts models, which are equally weighted to derive a 12-month price target of A$2.5 per share. By applying the conversion rate of 1 ADR = 10 Kazia common shares and an exchange rate of A$1.00 to $0.73, we arrive at our 12-month US price target of $18 per ADS (American Depository Share).

Exhibit 29. Free Cash Flow Model.

Average (AUD)	$2.4	Price/Share
Price Target (USD)	**$18**	Price/Share

DCF Valuation Using FCF (mln):

	2019	2020	2021	2022	2023	2024	2025	2026	2027	2028	2029	2030	2031
units AUD ('000)	**2019A**	**2020E**	**2021E**	**2022E**	**2023E**	**2024E**	**2025E**	**2026E**	**2027E**	**2028E**	**2029E**	**2030E**	**2031E**
EBIT	(10,270)	(12,467)	(8,422)	(24,798)	(28,517)	(17,517)	13,680	73,864	106,111	165,101	343,292	505,389	661,924
Tax Rate	0%	0%	0%	0%	0%	0%	0%	0%	0%	5%	5%	8%	8%
EBIT (1-t)	(10,270)	(12,467)	(8,422)	(24,798)	(28,517)	(17,517)	13,680	73,864	106,111	156,846	326,128	464,958	608,971
CapEx	-	-	-	-	-	-	-	-	-	-	-	-	-
Depreciation	1,084	-	-	-	-	-	-	-	-	-	-	-	-
Change in NWC													
FCF	(9,186)	(12,467)	(8,422)	(24,798)	(28,517)	(17,517)	13,680	73,864	106,111	156,846	326,128	464,958	608,971
PV of FCF	(15,524)	(16,208)	(8,422)	(19,075)	(16,874)	(7,973)	4,790	19,894	21,984	24,996	39,980	43,845	44,174
Discount Rate	30%												
Long Term Growth Rate	1%												
Terminal Cash Flow	2,120,897												
Terminal Value YE2031	153,846												
NPV	284,955												
NPV-Debt	-												
Shares out ('000)	135,024	2031E											
NPV Per Share	2												

Source: Maxim estimates.

Exhibit 30. Discounted-EPS Model.

Current Year	2021
Year of EPS	2031
Earnings Multiple	10
Discount Factor	30%
Selected Year EPS	4.51
NPV	3

Source: Maxim estimates.

	Discount Rate and Earnings Multiple Varies, Year is Constant						
	3.27	**5%**	**10%**	**15%**	**20%**	**25%**	**30%**
Earnings Multiple	**0**	0	0	0	0	0	0
	5	13.84	8.69	5.57	3.64	2.42	1.64
	10	27.69	17.39	11.15	7.28	4.84	3.27
	15	41.53	26.08	16.72	10.93	7.26	4.91
	20	55.38	34.78	22.30	14.57	9.69	6.54
	25	69.22	43.47	27.87	18.21	12.11	8.18
	30	83.06	52.17	33.44	21.85	14.53	9.81
	35	96.91	60.86	39.02	25.49	16.95	11.45

Exhibit 31. Sum-of-the-Parts Model.

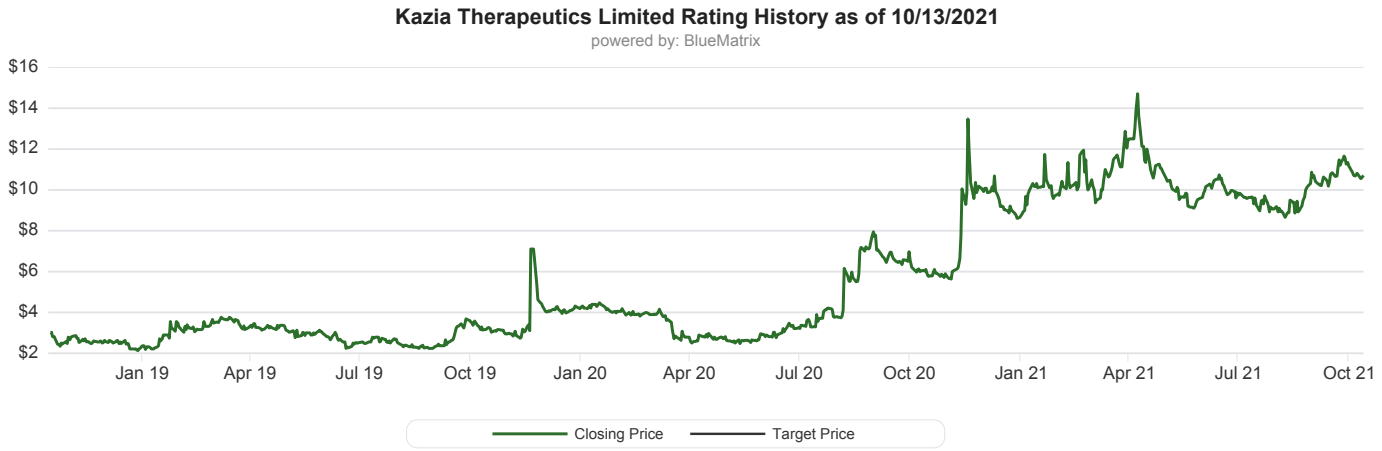
Kazia Therapeutics (KZIA)	LT Gr	Discount Rate	Yrs to Mkt	% Success	Peak Sales (MM's)	Term Value
Paxalisib - GBM (US)	1%	30%	3	55%	$229	$789
NPV						$0.80
Paxalisib - GBM (Royalty)	1%	30%	3	55%	$47	$161
NPV						$0.16
Paxalisib - Brain mets (US)	1%	30%	5	45%	$445	$1,534
NPV						$1
Paxalisib - Brain mets (Royalty)	1%	30%	6	45%	$87	$299
NPV						$0.11
Net Margin						55%
MM Shrs OS (2031E)						135
Total						$2

Source: Maxim estimates.

Kazia Therapeutics Limited (KZIA) Income Statement (A$000) YE June 30	2018A	FY 2019A	FY 2020A	July-Dec 1H21A	Jan-Jun 2H21A	FY 2021A	FY 2022E	FY 2023E	FY 2024E	FY 2025E	FY 2026E	FY 2027E	FY 2028E	FY 2029E	FY 2030E	FY 2031E
Product Revenue:																
Paxalisib - GBM (US)			-	-	-	-	-	-	13,865	25,523	36,812	48,759	83,719	114,996	130,316	228,837
Paxalisib - Brain Mets (US)			-	-	-	-	-	-	-	23,259	57,507	74,054	101,721	261,982	377,851	444,871
Net revenue	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**13,865**	**48,782**	**94,318**	**122,813**	**185,439**	**376,978**	**508,167**	**673,709**
Collaborative revenue:																
Paxalisib - GBM *(Royalties)*									2,760	7,592	14,843	20,852	22,913	32,458	35,858	46,608
Paxalisib - Brain Mets *(Royalties)*										-	18,151	23,322	31,965	49,288	79,627	86,804
Other income		1,465	995	1	15,184	15,185										
Finance Income		100	66	31	11	42	-	-	-	-	-	-	-	-	-	-
		-	-			-	-	-	-	-	-	-	-	-	-	-
Total Collaborative Revenue	**-**	**1,565**	**1,061**	**32**	**15,195**	**15,227**	**-**	**-**	**2,760**	**7,592**	**32,994**	**44,174**	**54,879**	**81,746**	**115,485**	**133,412**
Total Revenue	**-**	**1,565**	**1,061**	**32**	**15,195**	**15,227**	**-**	**-**	**16,625**	**56,374**	**127,312**	**166,987**	**240,318**	**458,724**	**623,652**	**807,120**
Gross Margins:																
Cost of Goods Sold									2,773	9,756	18,864	24,563	37,088	75,396	76,225	101,056
Gross Profit	**-**	**1,565**	**1,061**	**32**	**15,195**	**15,227**	**-**	**-**	**13,852**	**46,617**	**108,448**	**142,424**	**203,230**	**383,328**	**547,427**	**706,064**
Operating Expenses:																
Research and Development		6,476	9,494	2,860	11,682	14,541	16,723	19,231	21,154	22,212	23,322	24,488	25,713	26,999	28,348	29,766
Selling, General and Administrative		3,786	3,690	3,576	3,446	7,022	8,075	9,286	10,215	10,726	11,262	11,825	12,416	13,037	13,689	14,374
Fair value losses on financial assets at fair value through profits or loss		1,809	168													
Loss on disposal of fixed assets		1														
Loss on revaluation of contingent considersation		63	**475**	**110**	**2,461**	**2,570**										
Total Expenses	**-**	**12,134**	**13,827**	**6,545**	**17,589**	**24,133**	**24,798**	**28,517**	**34,142**	**42,694**	**53,448**	**60,876**	**75,217**	**115,431**	**118,263**	**145,196**
Operating Income (Loss)	**-**	**(10,568)**	**(12,766)**	**(6,513)**	**(2,394)**	**(8,906)**	**(24,798)**	**(28,517)**	**(17,517)**	**13,680**	**73,864**	**106,111**	**165,101**	**343,292**	**505,389**	**661,924**
		-	-			-	-	-	-	-	-	-	-	-	-	-
Income tax benefit		298	298	149	335	484	-	-	-	-	-	-	-	-	-	-
		-	-			-	-	-	-	-	-	-	-	-	-	-
		-	-			-	-	-	-	-	-	-	-	-	-	-
		-	-			-	-	-	-	-	-	-	-	-	-	-
		-	-			-	-	-	-	-	-	-	-	-	-	-
Total Other Income	**-**	**298**	**298**	**149**	**335**	**484**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**	**-**
Pretax Income	**-**	**(10,270)**	**(12,467)**	**(6,364)**	**(2,058)**	**(8,422)**	**(24,798)**	**(28,517)**	**(17,517)**	**13,680**	**73,864**	**106,111**	**165,101**	**343,292**	**505,389**	**661,924**
Taxes on income		-	-	-	-	-	-	-	-	-	-	-	8,255	17,165	40,431	52,954
Tax Rate													*5%*	*5%*	*8%*	*8%*
GAAP Net Income (Loss)	**-**	**(10,270)**	**(12,467)**	**(6,364)**	**(2,058)**	**(8,422)**	**(24,798)**	**(28,517)**	**(17,517)**	**13,680**	**73,864**	**106,111**	**156,846**	**326,128**	**464,958**	**608,971**
Net exchange difference on translation of financial statements of foreign controlled entities		(88.986)	(4)	1	1	2										
Total comprehensive loss	**-**	**(10,359)**	**(12,471)**	**(6,362)**	**(2,058)**	**(8,420)**	**(24,798)**	**(28,517)**	**(17,517)**	**13,680**	**73,864**	**106,111**	**156,846**	**326,128**	**464,958**	**608,971**
GAAP-EPS	#DIV/0!	(0.18)	(0.17)	(0.06)	(0.02)	(0.07)	(0.19)	(0.21)	(0.13)	0.10	0.55	0.79	1.17	2.43	3.45	4.51
GAAP-EPS (Dil)	#DIV/0!	(0.18)	(0.17)	(0.06)	(0.02)	(0.07)	(0.19)	(0.21)	(0.13)	0.10	0.55	0.79	1.17	2.43	3.45	4.51
Wgtd Avg Shrs (Bas) - '000s	-	57,504	73,054	107,422	127,927	117,675	130,120	132,882	133,148	133,414	133,681	133,949	134,217	134,485	134,754	135,024
Wgtd Avg Shrs (Dil) - '000s	-	57,504	73,054	107,422	127,927	117,675	130,120	132,882	133,148	133,414	133,681	133,949	134,217	134,485	134,754	135,024

Source: Company reports and Maxim

DISCLOSURES



Maxim Group LLC Ratings Distribution		As of: 10/13/21	
		% of Coverage Universe with Rating	% of Rating for which Firm Provided Banking Services in the Last 12 months
Buy	Fundamental metrics and/or identifiable catalysts exist such that we expect the stock to outperform its relevant index over the next 12 months.	**88%**	**55%**
Hold	Fundamental metrics are currently at, or approaching, industry averages. Therefore, we expect this stock to neither outperform nor underperform its relevant index over the next 12 months.	**12%**	**46%**
Sell	Fundamental metrics and/or identifiable catalysts exist such that we expect the stock to underperform its relevant index over the next 12 months.	**0%**	**0%**
	**See valuation section for company specific relevant indices*		

I, Naureen Quibria, Ph.D., attest that the views expressed in this research report accurately reflect my personal views about the subject security and issuer. Furthermore, no part of my compensation was, is, or will be directly or indirectly related to the specific recommendation or views expressed in this research report.

The research analyst(s) primarily responsible for the preparation of this research report have received compensation based upon various factors, including the firm's total revenues, a portion of which is generated by investment banking activities.

Maxim Group makes a market in Kazia Therapeutics Limited

Maxim Group expects to receive or intends to seek compensation for investment banking services from Kazia Therapeutics Limited in the next 3 months.

KZIA: For Kazia Therapeutics Limited, we use the BTK (NYSE Biotechnology Index) as the relevant index.

Valuation Methods

KZIA: We model the launch of paxalisib in GBM in the US, EU and China in CY24; and in brain metastases in the US in CY25 and in the EU and China in CY26, with a 70% risk adjustment. A 30% discount is applied to the free cash flow, discounted EPS, and sum-of-the-parts models, which are equally weighted to derive a 12-month price target.

Price Target and Investment Risks

KZIA: Aside from general market and other economic risks, risks particular to our price target and rating for Kazia Therapeutics Limited include: (1) the regulatory and clinical risk associated with product development; (2) the rate and degree of progress of product development; (3) the rate of regulatory approval and timelines to potential commercialization of products; (4) the level of success achieved in clinical trials; (5) the requirements for marketing authorization from regulatory bodies in the United States and other countries; (6) the liquidity and market volatility of

the company's equity securities; (7) regulatory and manufacturing requirements and uncertainties; (8) product and technology developments by competitors, potentially with more resources and commercial infrastructure; (9) inability, of product(s), if approved, to gain adequate market share and maintain adequate revenue growth; (10) impact of comprehensive tax reform in the US and Ex-US tax policy; (11) delays related to COVID-19 could impact the company's ability to operate and conduct clinical trials; (12) failure of third-parties to meet contractual obligations, potentially impacting drug development; (13) the ability to access capital via equity financing or convertible debt securities, which will likely have a dilutive effect on shareholders; (14) foreign exchange fluctuations as the company is domiciled in Australia and reports results in AUD.

RISK RATINGS

Risk ratings take into account both fundamental criteria and price volatility.

Speculative – Fundamental Criteria: This is a risk rating assigned to early-stage companies with minimal to no revenues, lack of earnings, balance sheet concerns, and/or a short operating history. Accordingly, fundamental risk is expected to be significantly above the industry. Price Volatility: Because of the inherent fundamental criteria of the companies falling within this risk category, the price volatility is expected to be significant with the possibility that the investment could eventually be worthless. Speculative stocks may not be suitable for a significant class of individual investors.

High – Fundamental Criteria: This is a risk rating assigned to companies having below-average revenue and earnings visibility, negative cash flow, and low market cap or public float. Accordingly, fundamental risk is expected to be above the industry. Price Volatility: The price volatility of companies falling within this category is expected to be above the industry. High-risk stocks may not be suitable for a significant class of individual investors.

Medium – Fundamental Criteria: This is a risk rating assigned to companies that may have average revenue and earnings visibility, positive cash flow, and is fairly liquid. Accordingly, both price volatility and fundamental risk are expected to approximate the industry average.

Low – Fundamental Criteria: This is a risk rating assigned to companies that may have above-average revenue and earnings visibility, positive cash flow, and is fairly liquid. Accordingly, both price volatility and fundamental risk are expected to be below the industry.

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