# Kazia Therapeutics

Development update

## EVT801 data published in peer-reviewed journal

Pharma and biotech

**Kazia Therapeutics has announced the publication of pre-clinical data for its second pipeline asset, EVT801 in the journal *Cancer Research Communications*. The research was conducted by licensing partner Evotec and was the key driver for Kazia in-licensing the asset in 2021. EVT801 is an inhibitor of vascular endothelial growth factor receptors (VEGFR), which play an important role in angiogenesis and lymphangiogenesis (processes that contribute to tumor growth and metastasis), making VEGFR a well-established therapeutic target. While VEGFR inhibitors have been on the market for over a decade, Kazia asserts that by selectively targeting VEGFR3, EVT801 offers a potent and less toxic therapeutic profile than other benchmark drugs, such as Novartis' Votrient (pazopanib) and Bayer's Nexavar (sorafenib). EVT801 is currently in a Phase I clinical trial with initial data expected in H1 CY23. Our valuation changes slightly to $143.9m or US$8.81 per basic ADR, reflecting the additional shares issued under the at-the-money (ATM) facility.**

| Year end | Revenue (US$m) | PBT* (US$m) | EPADR (US$) | DPADR (US$) | P/E (x) | Gross yield (%) |
|---|---|---|---|---|---|---|
| 06/21 | 10.5 | (3.1) | (0.25) | 0.0 | N/A | N/A |
| 06/22 | 0.0 | (14.6) | (1.08) | 0.0 | N/A | N/A |
| 06/23e | 0.0 | (18.6) | (1.12) | 0.0 | N/A | N/A |
| 06/24e | 10.6 | (16.8) | (1.01) | 0.0 | N/A | N/A |

Note: *Converted at 1.45/US$. Dividend yield excludes withholding tax. Investors should consult their tax advisor regarding the application of any domestic and foreign tax laws.

## A specific inhibitor of VEGFR3

The VEGFR family of proteins are receptor tyrosine kinases and in cancer are implicated in angiogenesis and lymphangiogenesis. These proteins have been a common target for therapeutics (such as the first-in-class angiogenesis inhibitor Avastin), although fewer efforts have been made to specifically target the VEGFR3 isoform, which is important for the formation of lymphatic vessel networks. Management believes that more selective VEGFR3 inhibition may result in improved drug tolerance and lessen development of resistance to therapy.

## Positive pre-clinical data on EVT801

The recently published pre-clinical data (both in vitro and in vivo) demonstrated that EVT801 was able to achieve strong anti-tumor activity in VEGFR3+ tumors even at low (nanomolar) dosages, suggesting a good safety profile and the potential for a wide therapeutic window. The drug also presented higher activity than currently marketed drugs pazopanib and sorafenib in in-vivo mouse models. Importantly, the drug showed synergistic efficacy benefits in combination with checkpoint inhibitors, which highlight incremental potential as a combination treatment.

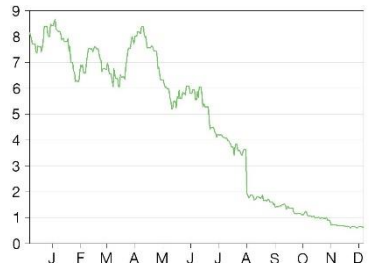
## Valuation: US$143.9m or US$8.81 per basic ADR

We update our valuation for the latest issues under the ATM facility, which we estimate has contributed c US$4m in funds in H123 to date for Kazia. Our revised valuation stands at US$143.9m or US$8.81 per basic ADR. We expect the upcoming top-line data for EVT801 in H1 CY23 to be a key share price catalyst.

**7 December 2022**

| | |
|---|---|
| **Price** | **$0.6** |
| **Market cap** | **$10m** |
| ADR/Ord conversion ratio | 1:10 |
| Net cash (US$m) at end-September 2022 | 3.4 |
| ADRs in issue | 16.34m |
| ADR code | KZIA |
| ADR exchange | Nasdaq |
| Underlying exchange | ASX |
| Depository | BNY |

### ADR share price performance




| 52-week high/low | $8.65 | $0.59 |
|---|---|---|

### Business description

Kazia Therapeutics is a late-stage clinical pharmaceutical company with lead asset paxalisib (a PI3K inhibitor that can cross the blood-brain barrier, licensed from Genentech) in a pivotal study for GBM and in early-stage studies in childhood brain cancers, DIPG and AT/RT. The other asset is the Phase I drug EVT801, an inhibitor of VEGFR3.

### Next events

| | |
|---|---|
| Interim data from EVT801 Phase I study | H1 CY23 |
| Phase III GBM AGILE top-line data | H2 CY23 |
| Interim data from Phase II PNOC22 trial | CY23 |

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# EVT801 – a selective inhibitor of VEGFR3

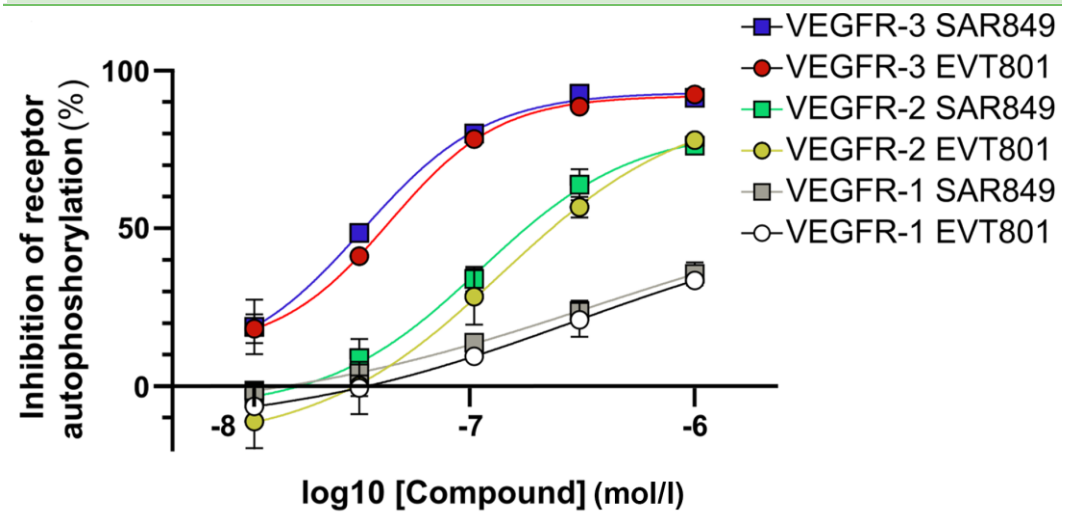
## VEGFR inhibitors' effectiveness in cancer limited by off-target activity

The role of VEGFR in tumorigenesis is well understood, with several drugs currently available on the market. In 2004, Avastin (bevacizumab) became the first drug to be approved in the category, pulling in sales of US$7.1bn in 2019 before going off-patent. However, despite established efficacy signals, treatment has been challenged by off-target activity of the approved treatments, which is widely attributed to their lack of selectivity. Side effects such as hypertension, anorexia and fatigue are commonly reported, leading to restrictions in therapeutic dosages. Moreover, broad-activity VEGFR inhibitors are believed to cause sustained tumor hypoxia, which may lead to cancer cells developing treatment resistance, adapting and proliferating further.

## EVT801 is highly VEGFR3 selective…

EVT801 has been positioned as a more selective, new-generation inhibitor with potentially fewer off-target effects, improved safety profile and capability to lower hypoxia-induced resistance (thereby higher treatment durability). In an in-vitro study using human embryonic kidney (HEK)293 cell lines expressing VEGFR1, 2 and 3, EVT801 and its active metabolite (SAR849) exhibited greater affinity for VEGFR3 over other isoforms (Exhibit 1). While pre-clinical data may not necessarily translate into a meaningful clinical effect, these early results are encouraging for EVT801's potential market differentiating VEGFR3 selectivity.

**Exhibit 1: EVT801's isoform selectivity**

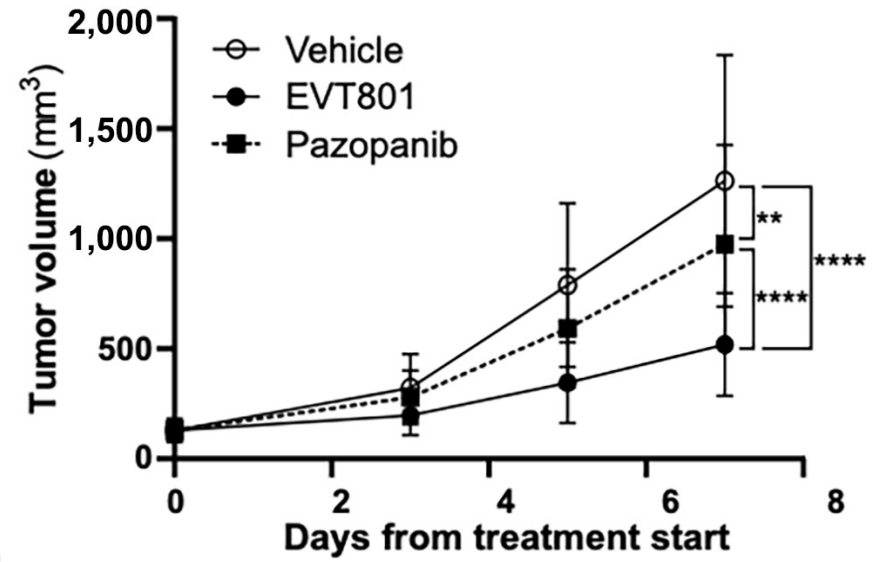



Source: Targeting Tumor Angiogenesis with the Selective VEGFR3 Inhibitor EVT801 in Combination with Cancer Immunotherapy. *Cancer Research Communications*

## …with superior pre-clinical activity over a competing treatment

In an additional in-vivo model using subcutaneous tumor xenografts, oral administration of 30mg/kg twice a day EVT801 demonstrated a significant inhibition of tumor growth compared to the pan-VEGFR inhibitor pazopanib (30mg/kg twice a day) or the vehicle/control (5ml/kg twice a day) over seven days of treatment (Exhibit 2). As a reminder, pazopanib is currently approved under the brand name Votrient, for the treatment of renal cell carcinoma and soft tissue sarcoma.

**Exhibit 2: EVT801's tumor growth inhibition versus benchmark**

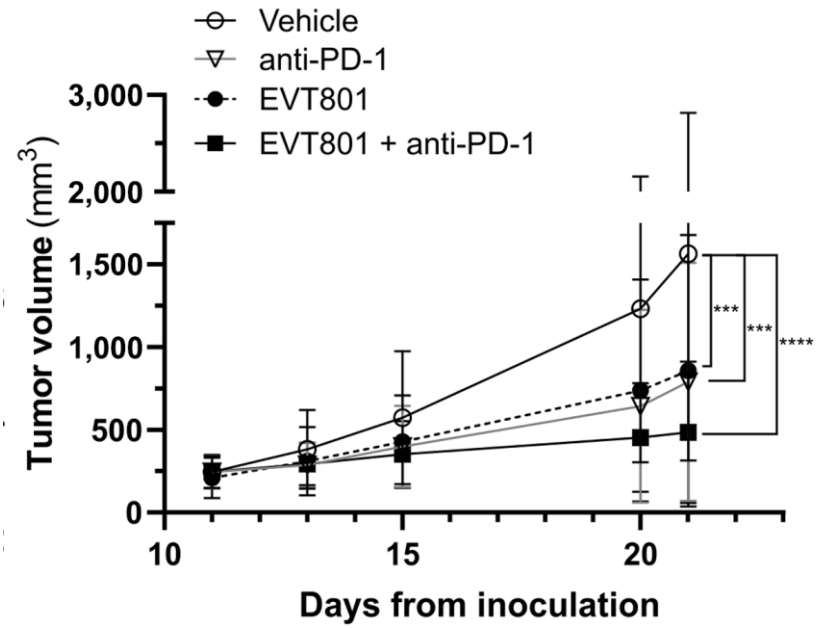



Source: Targeting Tumor Angiogenesis with the Selective VEGFR3 Inhibitor EVT801 in Combination with Cancer Immunotherapy. *Cancer Research Communications.*

## Potential as combination treatment with immunotherapy

Recent focus in cancer drug development has been on utilizing combination treatments to enhance the efficacy of monotherapies. Mouse model studies across several tumor types testing EVT801 in combination with immune checkpoint inhibitors showed strongly synergistic activity, with the combination performing better than either drug alone. While EVT801 monotherapy activity on tumor volumes was largely similar to the anti-PD-1 antibody, the combination treatment resulted in much lower levels of tumor progression, implying additional benefits (Exhibit 3). In our view, combination therapies will be critical for clinical breakthroughs in oncology, so we see this result as being highly supportive for the pursuit of the EVT801/immune checkpoint inhibitor combination in the clinic.

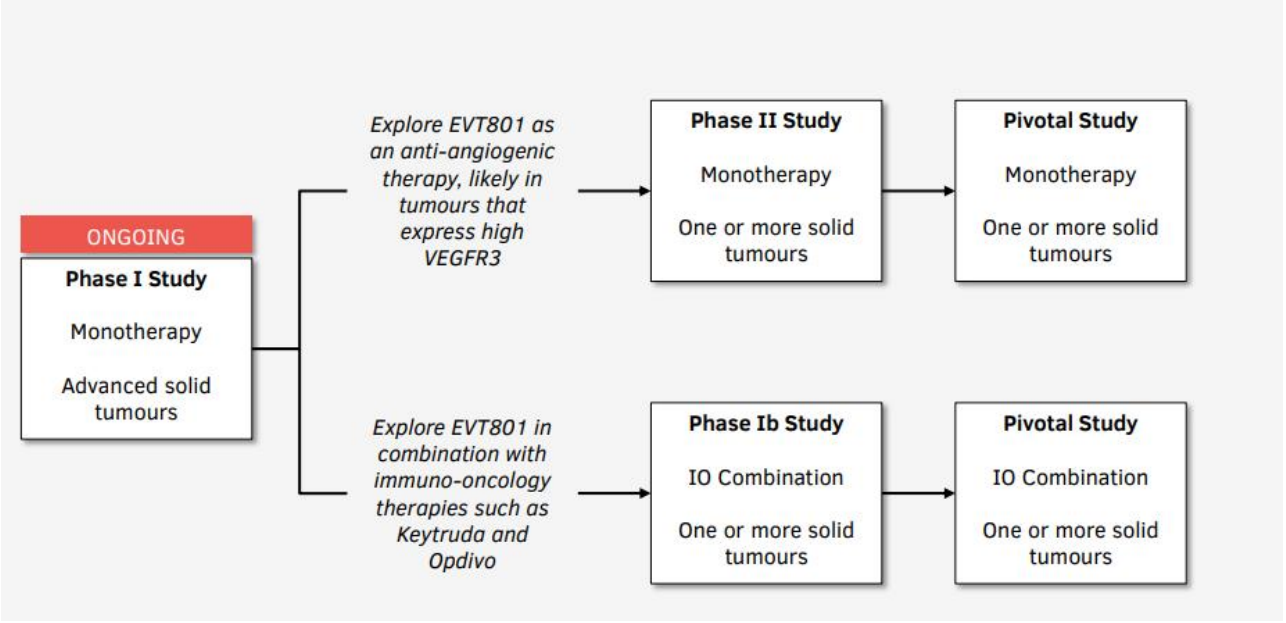
**Exhibit 3: EVT801's potential as combination treatment**




Source: Targeting Tumor Angiogenesis with the Selective VEGFR3 Inhibitor EVT801 in Combination with Cancer Immunotherapy. *Cancer Research Communications.*

EVT801 is currently undergoing a Phase I clinical trial as a monotherapy in patients with advanced solid tumors (NCT05114668). We expect Kazia to explore EVT801's potential as a combination treatment with checkpoint inhibitors as clinical development progresses (Exhibit 4 highlights the development strategy for EVT801). The Phase I study is expected to report initial data in H1 CY23 and we expect this could be a key share price catalyst for the company.

**Exhibit 4: EVT801's development strategy**




Source: Kazia Therapeutics corporate deck

# Financials and valuation

We update our FY23 and FY24 EPS estimates following two capital raises under the ATM facility in October 2022 (13.0m shares/1.3m ADRs for gross proceeds of US$1.56m). The September-end cash balance stood at US$3.4m and the equity proceeds take the updated pro-forma net cash to c US$5.0m (versus our previous estimate of US$7.6m). This results in our overall valuation coming down slightly to US$143.9m versus US$146.6m previously. The per ADR valuation gets affected further on account of the higher number of shares/ADRs outstanding following the issue, falling to US$8.81/ADR from US$9.79/ADR previously. A breakdown of our valuation is presented in Exhibit 5.

**Exhibit 5: Kazia Therapeutics valuation breakdown**

| Development Program | Indication | Clinical stage | Prob. of success | Launch year | Patent/Exclusivity Protection | Launch Pricing ($/course) | Peak sales (US$m) | rNPV (US$m) |
|---|---|---|---|---|---|---|---|---|
| Paxalisib | GBM | Phase II/III | 20% | 2025 | 2037 | 169,000 | 270 | 81.5 |
| | BCBMs | Phase II | 5% | 2029 | 2037 | 183,000 | 249 | 6.0 |
| Cantrixil | OC | Phase I complete | 15% | 2027 | 2040 | 124,000 | 174 | 7.5 |
| EVT801 | RCC | Phase I | 10% | 2028 | 2037 | 120,000 | 807 | 43.9 |
| **Total** | | | | | | | | **138.9** |
| Net cash and equivalents (end-September 2022+equity offering) (US$m) | | | | | | | | 4.96 |
| **Total firm value (US$m)** | | | | | | | | **143.91** |
| Total basic ADRs (m) | | | | | | | | 16.34 |
| **Value per basic ADR (US$)** | | | | | | | | **8.81** |

Source: Edison Investment Research

## Exhibit 6: Financial summary

| USD'000s | 2021 | 2022 | 2023e | 2024e |
|---|---|---|---|---|
| 30-June | IFRS | IFRS | IFRS | IFRS |
| INCOME STATEMENT | | | | |
| Revenue | 10,501.5 | 18.7 | 0.0 | 10,620.7 |
| Cost of Sales | 0.0 | 0.0 | 0.0 | (1,149.0) |
| Gross Profit | 10,501.5 | 18.7 | 0.0 | 9,471.7 |
| R&D | 10,028.5 | 13,967.0 | 17,669.0 | 20,420.7 |
| SG&A | 4,842.6 | 3,111.4 | 3,480.9 | 8,378.1 |
| EBITDA | (3,058.2) | (14,558.0) | (18,648.1) | (16,825.3) |
| Operating profit (before amort. and excepts.) | (3,058.2) | (14,558.0) | (18,648.1) | (16,825.3) |
| Amortisation of acquired intangibles | (872.6) | (1,346.9) | (1,346.9) | (1,346.9) |
| Exceptionals | (1,772.6) | (192.6) | 0.0 | 0.0 |
| Share-based payments | (438.9) | (1,154.9) | (1,154.9) | (1,154.9) |
| Reported operating profit | (6,142.3) | (17,252.3) | (21,149.8) | (19,327.0) |
| Net Interest | 0.0 | 0.0 | 0.0 | 0.0 |
| Joint ventures & associates (post tax) | 0.0 | 0.0 | 0.0 | 0.0 |
| Exceptionals | 0.0 | 0.0 | 0.0 | 0.0 |
| Profit Before Tax (norm) | (3,058.2) | (14,558.0) | (18,648.1) | (16,825.3) |
| Profit Before Tax (reported) | (6,142.3) | (17,252.3) | (21,149.8) | (19,327.0) |
| Reported tax | 334.0 | 253.8 | 311.2 | 284.4 |
| Profit After Tax (norm) | (2,891.9) | (14,343.8) | (18,373.7) | (16,577.7) |
| Profit After Tax (reported) | (5,808.2) | (16,998.5) | (20,838.6) | (19,042.7) |
| Minority interests | 0.0 | 0.0 | 0.0 | 0.0 |
| Discontinued operations | 0.0 | 0.0 | 0.0 | 0.0 |
| Net income (normalised) | (2,891.9) | (14,343.8) | (18,373.7) | (16,577.7) |
| Net income (reported) | (5,808.2) | (16,998.5) | (20,838.6) | (19,042.7) |
| Average Number of Shares Outstanding (m) | 11.8 | 13.2 | 16.3 | 16.3 |
| EPS - normalised (c) | (0.25) | (1.08) | (1.12) | (1.01) |
| EPADR - diluted normalised (US$) | (0.25) | (1.08) | (1.12) | (1.01) |
| EPADR - basic reported (US$) | (0.49) | (1.28) | (1.28) | (1.17) |
| Dividend (A$) | 0.00 | 0.00 | 0.00 | 0.00 |
| **BALANCE SHEET** | | | | |
| Fixed Assets | 19,790.5 | 18,862.4 | 16,136.3 | 13,410.1 |
| Intangible Assets | 15,174.2 | 13,827.3 | 12,480.5 | 11,133.6 |
| Tangible Assets | 0.0 | 0.0 | 0.0 | 0.0 |
| Investments & other | 4,616.3 | 5,035.1 | 3,655.8 | 2,276.5 |
| Current Assets | 20,269.5 | 5,247.1 | 8,003.4 | 15,416.4 |
| Stocks | 0.0 | 0.0 | 0.0 | 283.3 |
| Debtors | 58.2 | 62.7 | 0.0 | 6,983.5 |
| Cash & cash equivalents | 19,025.4 | 5,076.6 | 7,895.7 | 8,042.0 |
| Other | 1,186.0 | 107.7 | 107.7 | 107.7 |
| Current Liabilities | (5,742.5) | (3,231.1) | (5,236.1) | (7,405.5) |
| Creditors | (3,401.8) | (2,593.2) | (4,598.2) | (6,767.5) |
| Tax and social security | 0.0 | 0.0 | 0.0 | 0.0 |
| Short term borrowings | 0.0 | 0.0 | 0.0 | 0.0 |
| Other | (2,340.6) | (638.0) | (638.0) | (638.0) |
| Long Term Liabilities | (8,213.6) | (8,024.4) | (21,506.3) | (41,911.5) |
| Long term borrowings | 0.0 | 0.0 | (13,793.1) | (34,482.8) |
| Other long term liabilities | (8,213.6) | (8,024.4) | (7,713.2) | (7,428.8) |
| Net Assets | 26,103.9 | 12,854.0 | (2,602.7) | (20,490.5) |
| Minority interests | 0.0 | 0.0 | 0.0 | 0.0 |
| Shareholders' equity | 26,103.9 | 12,854.0 | (2,602.7) | (20,490.5) |
| **CASH FLOW** | | | | |
| Operating Cash Flow | (3,058.2) | (14,558.0) | (18,648.1) | (16,825.3) |
| Working capital | (3,855.7) | (72.5) | 3,135.8 | (4,002.5) |
| Exceptional & other | 630.8 | (1,067.9) | 311.2 | 284.4 |
| Tax | 0.0 | 0.0 | 0.0 | 0.0 |
| Net operating cash flow | (6,283.1) | (15,698.4) | (15,201.1) | (20,543.4) |
| Capex | 0.0 | 0.0 | 0.0 | 0.0 |
| Acquisitions/disposals | 0.0 | 0.0 | 0.0 | 0.0 |
| Net interest | 0.0 | 0.0 | 0.0 | 0.0 |
| Equity financing | 19,385.4 | 2,569.8 | 4,227.0 | 0.0 |
| Dividends | 0.0 | 0.0 | 0.0 | 0.0 |
| Other | 0.0 | (1,630.8) | 0.0 | 0.0 |
| Net Cash Flow | 13,102.3 | (14,759.5) | (10,974.0) | (20,543.4) |
| Opening net debt/(cash) | (6,234.3) | (19,215.4) | (5,266.7) | 5,707.3 |
| FX | (121.1) | 810.7 | 0.0 | 0.0 |
| Other non-cash movements | 0.0 | 0.0 | 0.0 | 0.0 |
| Closing net debt/(cash) | (19,215.4) | (5,266.7) | 5,707.3 | 26,250.7 |

Source: Kazia Therapeutics company accounts, Edison Investment Research

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