KAZIA THERAPEUTICS

A Diversified, Clinical-Stage Oncology Drug Development Company

EVT801: A clinical stage, first-in-class small molecule targeting tumor (lymph)-angiogenesis

Non-confidential deck

May 2024

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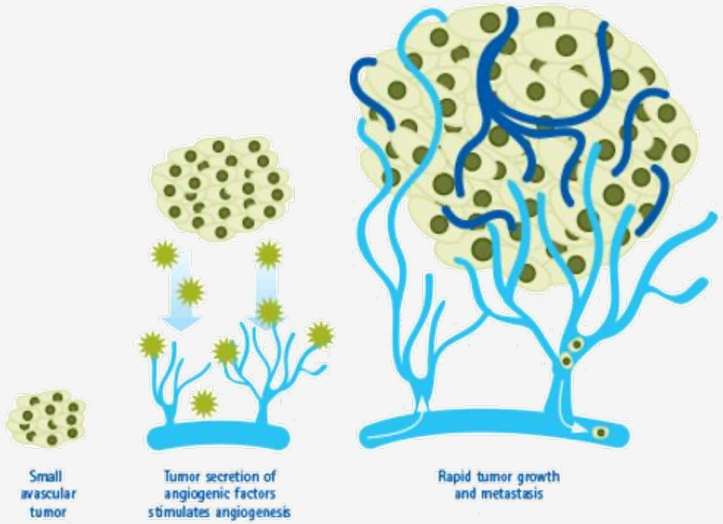
Targeting angiogenesis is a well-established approach in the treatment of cancer

Product	Company	Target	Indications	Annual Sales (US$)*
AVASTIN bevacizumab 100 MG/4 ML INJECTION FOR IV USE	Genentech A Member of the Roche Group	VEGF-A	• Colorectal cancer • Lung cancer • Breast cancer • Other cancers	**$7 billion**
Nexavar (sorafenib) tablets	BAYER	VEGFRs PDGFRs RAF kinases	• Hepatocellular carcinoma • Renal cell carcinoma • Thyroid cancer	**$1 billion**
SUTENT capsules sunitinib malate	Pfizer	VEGFRs PDGFRs	• Renal cell carcinoma • Gasto-intestinal stromal tumour	**$750 million**
Votrient pazopanib tablets (200 mg)	NOVARTIS	VEGFRs PDGFRs c-Kit FGFRs	• Renal cell carcinoma • Soft tissue sarcoma	**$1 billion**
Inlyta axitinib 1mg and 5mg tablets	Pfizer	VEGFRs c-Kit PDGFRs	• Renal cell carcinoma	**$400 million**

*approximate, based on company filings and market data

Despite their proven efficacy, angiogenesis inhibitors are limited by several key challenges

Angiogenesis inhibitors work by reducing the formation of **new blood vessels** around the tumour, starving it of vital nutrients needed for tumour growth, and limiting its ability to spread elsewhere in the body



1

Tumour Hypoxia

Sustained tumour hypoxia activates adaptive mechanisms, leading to secondary resistance and tumour progression

→ **Limited Duration of Effect**

2

Off-Target Activity

Most small molecule angiogenesis inhibitors have a broad range of pharmacological activities, leading to substantial toxicity (e.g. hypertension proteinuria & hand-foot syndrome)

→ **Significant Side Effects**

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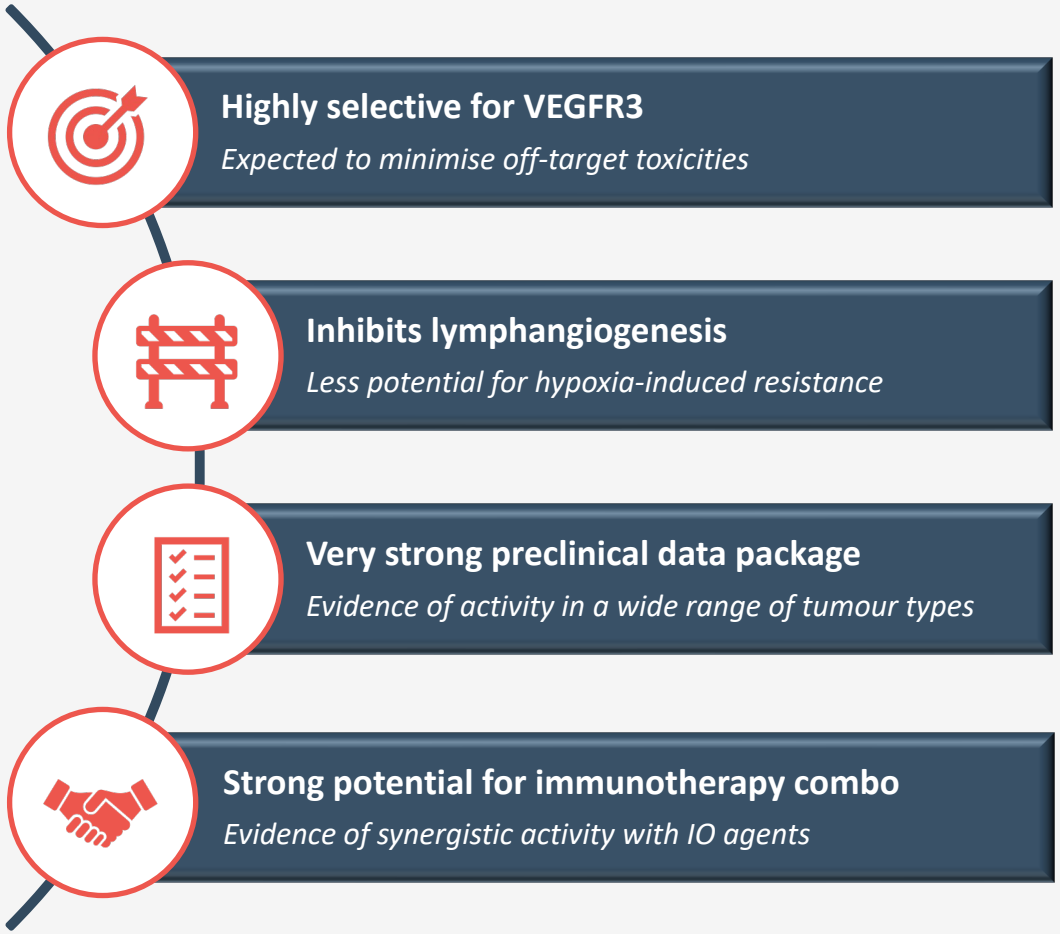
EVT801 is a highly selective VEGFR3 inhibitor, primarily inhibiting lymphangiogenesis (formation of new lymphatic vessels)



Oral Presentation

Administered by mouth once or twice daily

Strong IP Protection

Composition-of-matter to 2032 / 2033 in most jurisdictions

Low Cost of Goods

Straightforward manufacture with excellent stability

Favourable Preclinical Toxicology

Limited evidence of toxicity in one-month GLP animal studies

In Clinical Development

Currently undergoing Phase 1 clinical trial in Europe – Stage 1 completed

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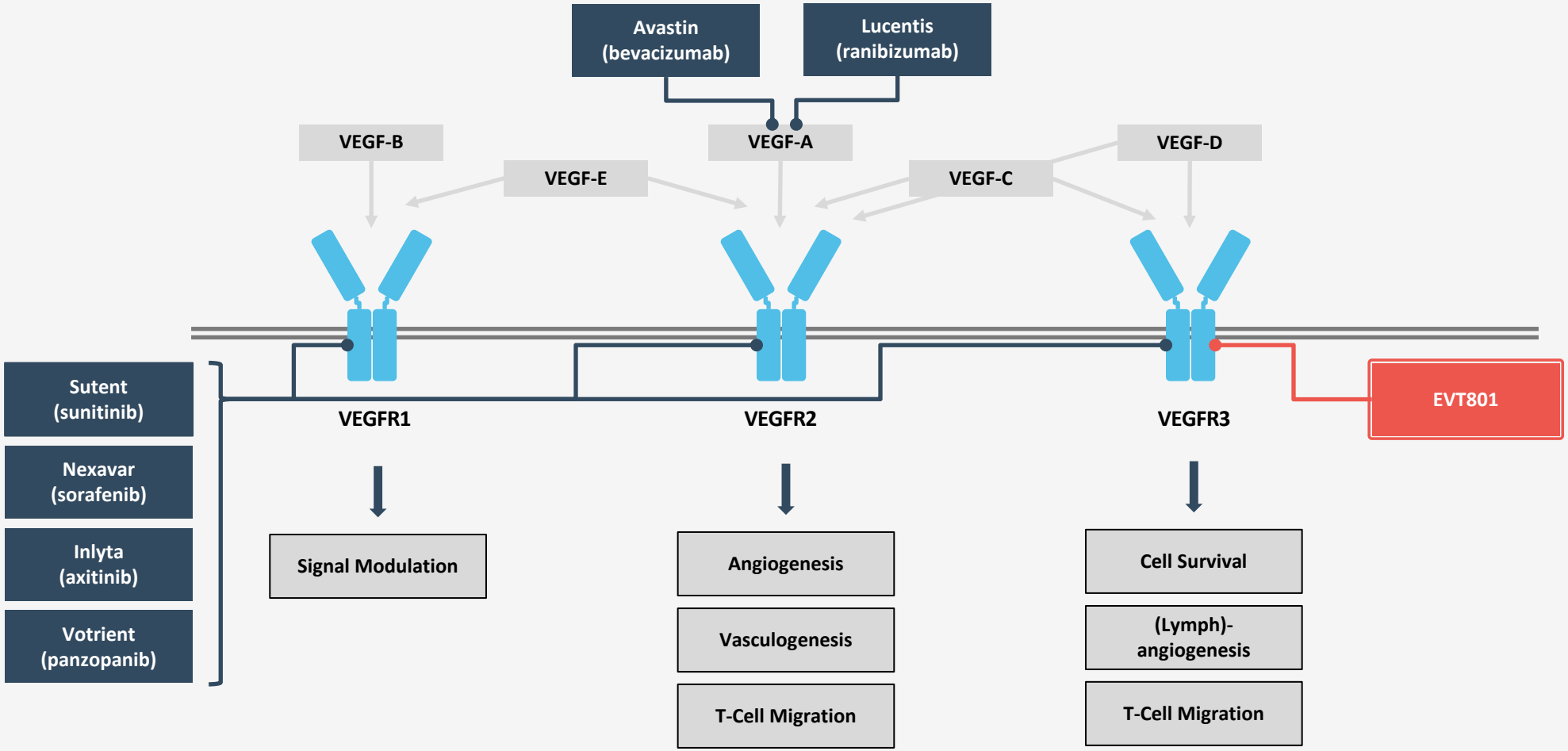
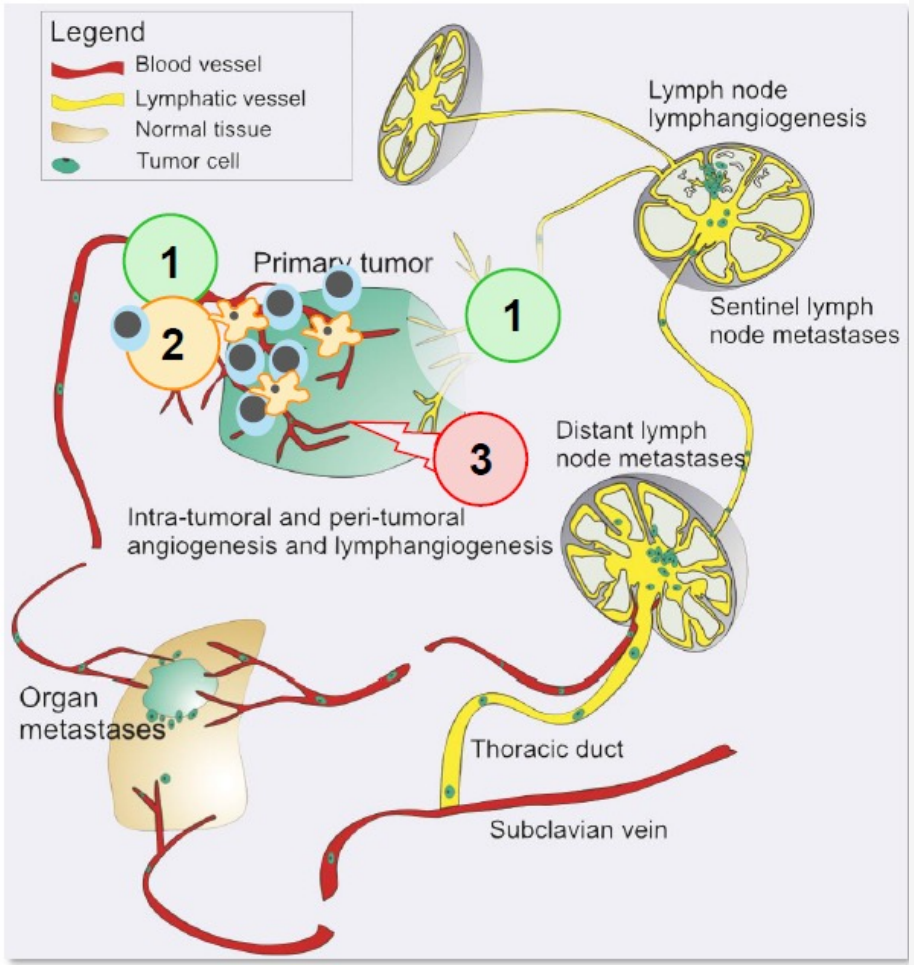
EVT801 selectively inhibits VEGFR3



EVT801: A differentiating anti-tumour approach



1

Inhibition of tumour escape and metastasis

- Stabilisation of tumour vasculature
- Inhibition of (lymph)-angiogenesis
- Avoidance of hypoxia decreases potential for metastatic spread

2

Increase in anti-tumour immune activity

- No impact on T-cells viability
- Increased infiltration of effector T-cells
- Reduction in immunosuppressive myeloid cells

3

Tumour Killing

- Direct effect on VEGFR3-expressing tumour cells (typically from endothelial origin, e.g. sarcoma)

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Preclinical data confirms activity of EVT801 (1/2)

Dramatic single-agent activity in DEN-induced Hepatocellular carcinoma model

Experimental Methods

- Syngeneic mouse model
- HCC chemically induced with diethylnitrosamine (DEN)
- Treatment with EVT801 in M10-M12

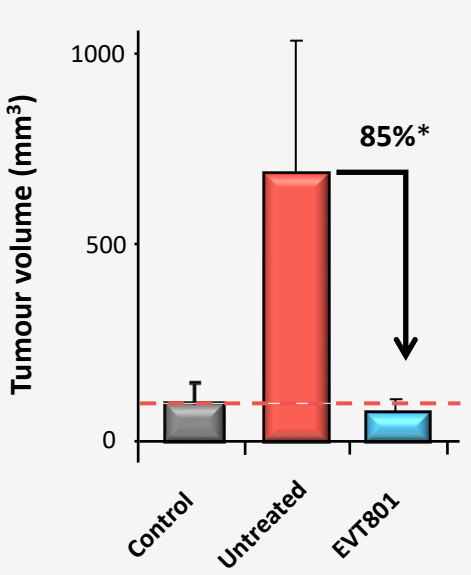
Conclusions

- EVT801 monotherapy causes marked reduction in growth of primary tumour versus untreated comparator
- EVT801 appears to have significant anti-metastatic effect

Tumour Growth

Total Tumour Volume

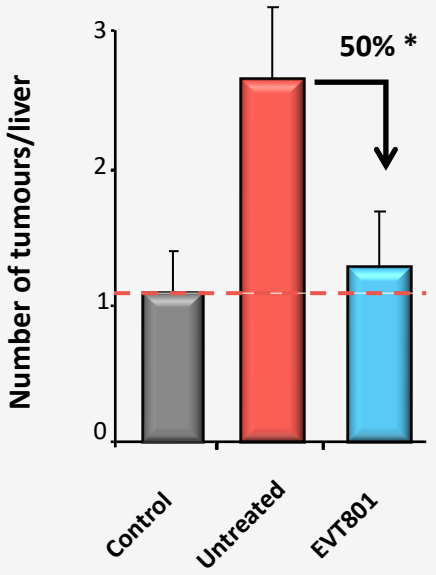
85% reduction



Metastasis

Number of Tumours in the Liver

50% reduction



* Statistically significant ($p<0.05$)

Data on file

Preclinical data confirms activity of EVT801 (2/2)

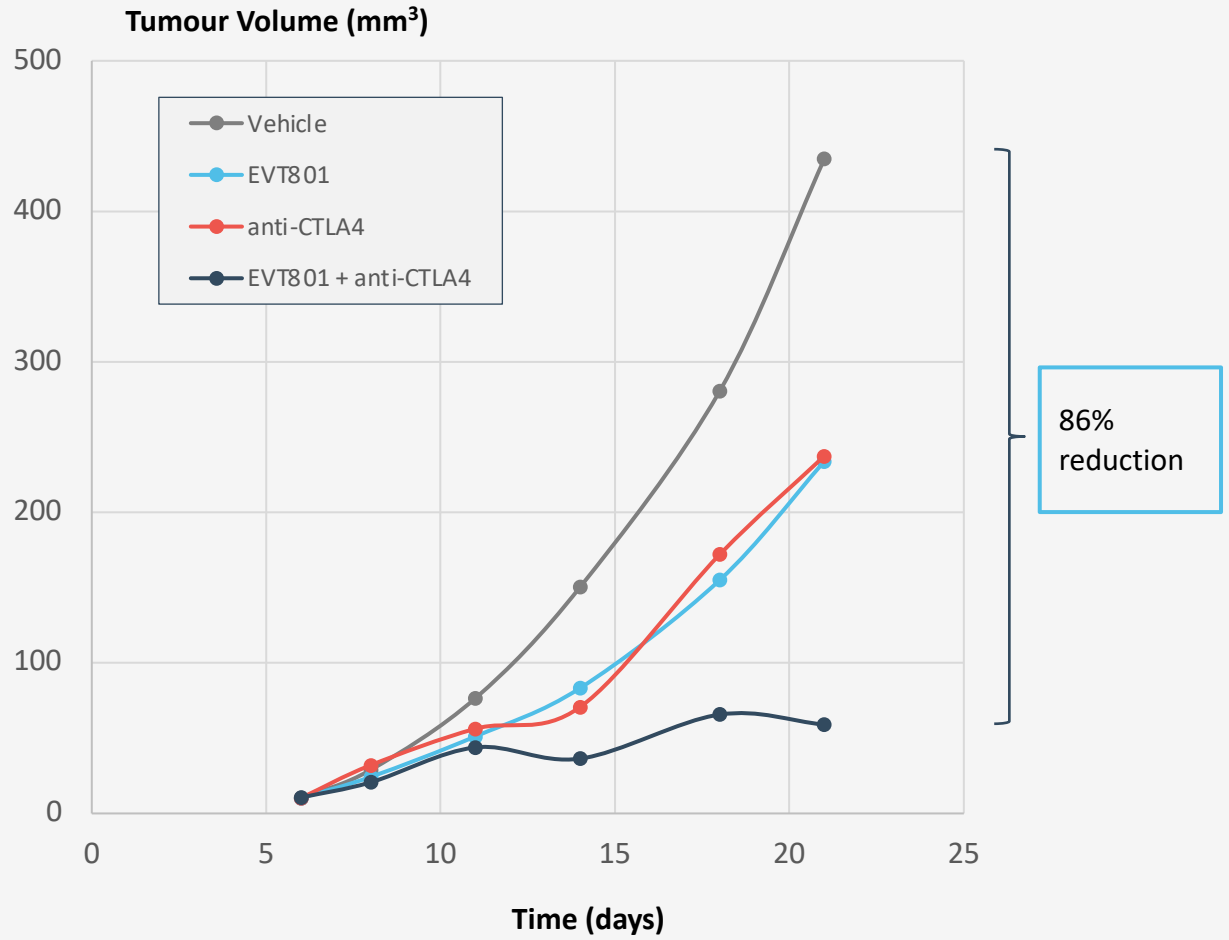
Synergistic activity in combination with anti-CTLA4 mAb

Experimental Methods

- Orthotopic tumour mouse model
- 4T1 tumour cells inoculated in BALB/c mice (mammary fat pad)
- Treatment with EVT801 on D7-D21 and with anti-CTLA4 on D7, D14, D21

Conclusions

- EVT801 monotherapy has approximately equivalent activity to anti-CTLA4 antibody
- Combination of EVT801 and anti-CTLA4 antibody is highly synergistic



Data on file

Note: CTLA4 is the target of Yervoy® (ipilimumab), an approved immuno-oncology therapy

Anti-tumour effects of EVT801

EVT801 preclinical data available upon request

- Shows strong *in vitro* activity on NCI-H1703 human lung cancer tumour cell line expressing VEGFR3
- Elicits potent *in vivo* efficacy on tumour cells expressing VEGFR-3
- More effective than pazopanib in rhabdomyosarcoma PDX model
- More active than pazopanib despite lower exposure
- Potent efficacy in a mouse xenograft NCI-H1703 cancer model

EVT801 is safer and has a unique mode of action compared to angiokinase inhibitors

Unique mode of action:

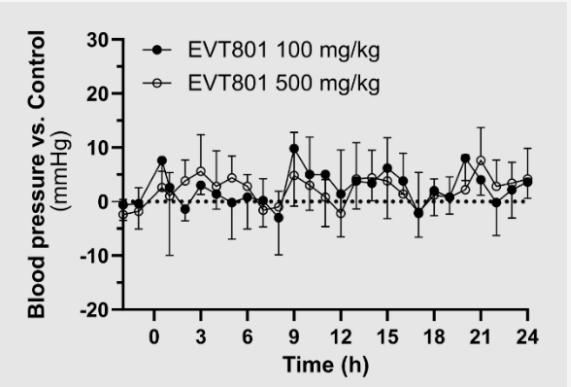
Characteristics	EVT801	Angiokinase inhibitors
Blood vessel normalization	• **Tumour blood vessel normalization through avoidance of hypoxia** decreases potential for metastatic spread	• Tumour escape due to only transient tumour blood vessel normalization inducing hypoxia
Immune activity	• **No impact on CD3⁺ T-cells proliferation** • **Reduction in immunosuppressive cells** (CD45+ PDL1+ & M2) • **Increase in pro-inflammatory macrophages** (M1)	• Inhibition of CD3⁺ T-cell proliferation • Increase in immunosuppressive cells • Decrease of pro-inflammatory macrophages (M1)

Safety:

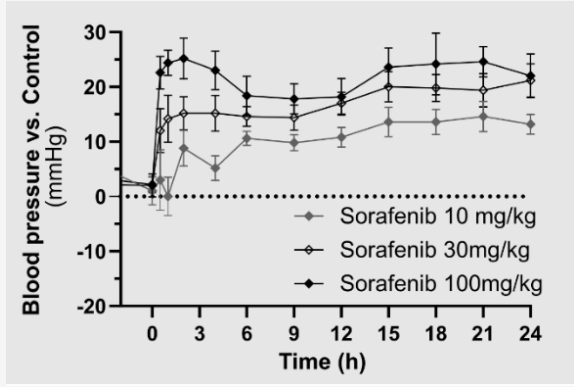
EVT801 does not induce hypertension in telemetered rats unlike sorafenib

- EVT801 does not induce any significant hypertension even after administration of 500mg/kg
- A singe administration of sorafenib from 10mg/kg produces dose-dependant and long-lasting increases in mean arterial pressure with a rapid onset of action

EVT801



Sorafenib



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EVT801 measures favorably against current anti-VEGF agents

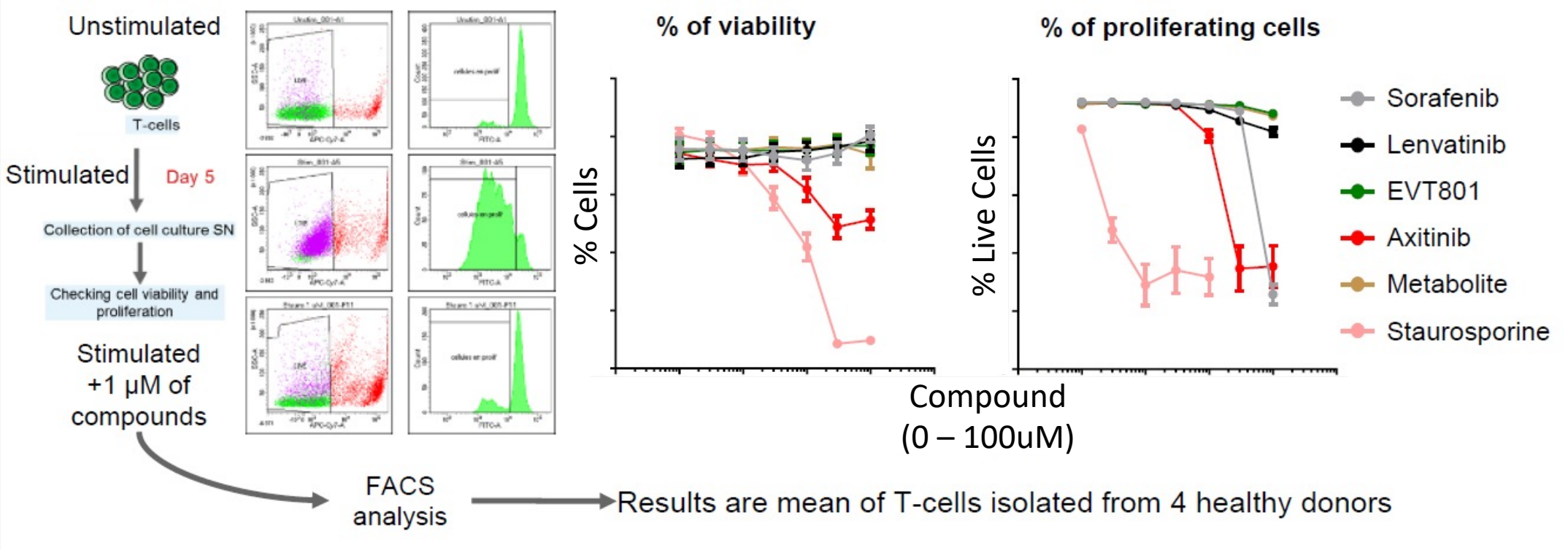
Target characteristic	EVT801	Multi-VEGF inhibitors
Potent small molecule VEGFR3 inhibitor	✓	✓
High selectivity over other VEGF receptors and TK panel	✓	X
Orally available	✓	✓
Effective as single agent in high VEGFR3 expression models	✓	✓
Potential companion diagnostic	✓	X
Equipotent to sorafenib	✓	✓
Reduced hypoxia/necrosis	✓	X
Well-tolerated in animal models	✓	✓
Reduce macrophage infiltration	✓	X
No inhibition of T cell function	✓	X
Potential for orphan status	✓	✓
Inhibits lymphangiogenesis	✓	X

Compound	Cellular *in vitro* IC_{50} (nM)	
	VEGFR2	VEGFR3
EVT801	**241**	**21**
EVT801 metabolite	**424**	**37**
Lenvatinib	58	390
Fruquintinib	568	2,097

- **More potent on VEGFR3** than second generation mTKIs
- **High cellular activity on VEGFR3** compared to key competitor compounds
- Active as single agent in range of models **without inducing hypoxia**
- Selective over GPCRs, ion channels, kinases
- **Negative** for Cytotoxicity, Ames, hERG, Cyp inhibition

Data comparing inhibition of T cell function is in the next slide , more differential data is available upon signing of a CDA

Unlike most mTKIs, EVT801 does not inhibit CD3+ T-cell function

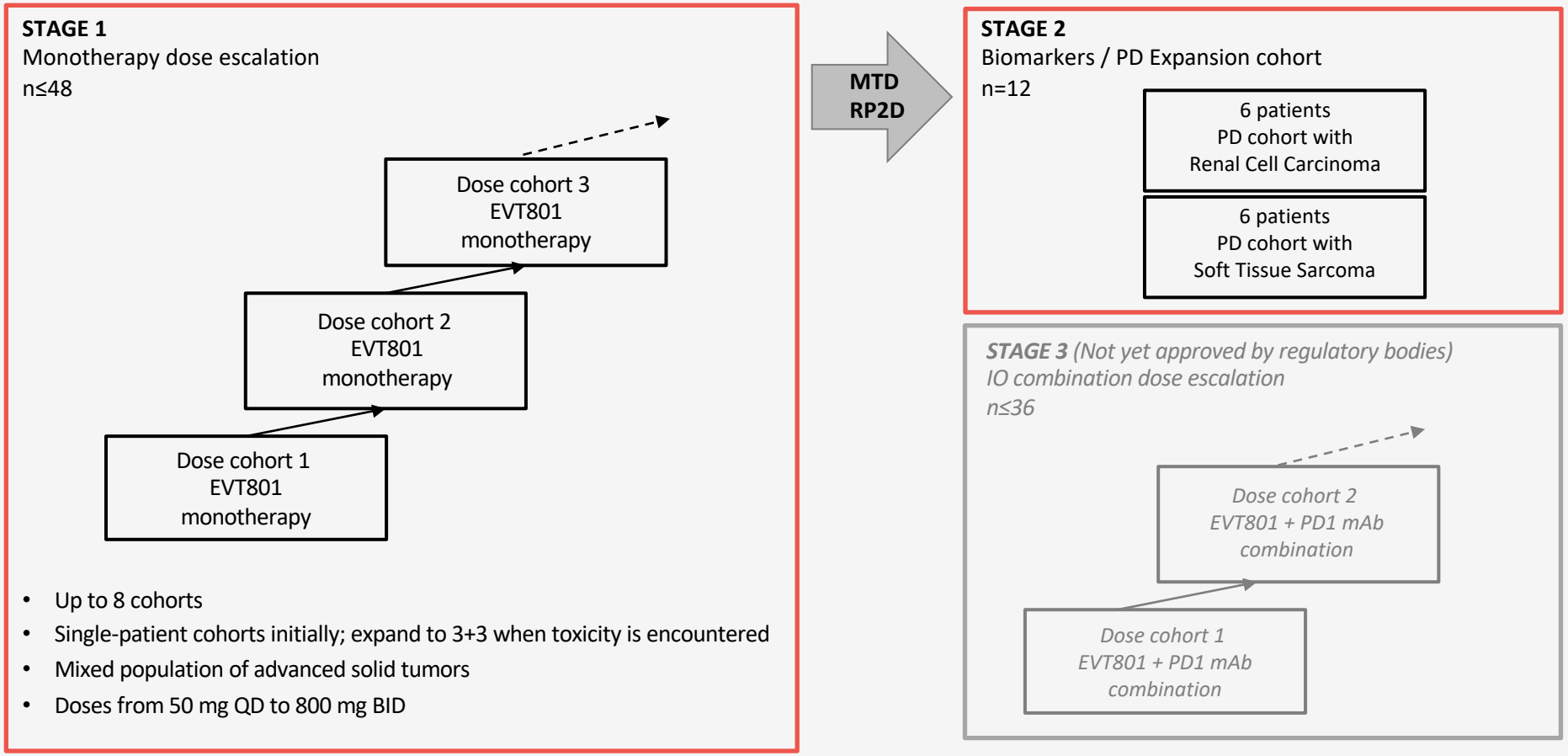


- Sorafenib and axitinib inhibit T-cell proliferation
- Similar to Lenvatinib, **EVT801 and its metabolite have no negative impact on T-cell viability and proliferation**

More differential data is available upon signing of a CDA

Phase 1 dose-finding trial ongoing in France – KZA 0801-101: *NCT05114668*

Target population: Histologically-confirmed advanced or metastatic solid tumours, unresponsive to standard treatment, or for whom no standard treatment is available or appropriate



Sponsor : Kazia Therapeutics Ltd

Product : EVT801

EudraCT Number : 2021-002483-47

Clinical sites (France only) :

- IUCT-Oncopole, Toulouse - PI : Dr Gomez-Roca
- Centre Léon Bérard, Lyon – PI : Dr Philippe Cassier

Stage 2: RCC: renal cell carcinoma; STS: soft tissue sarcoma; High grade serous (HGS) ovarian cancer under consideration

MTD = Most Tolerated Dose ; RP2D = Recommended Phase 2 Dose

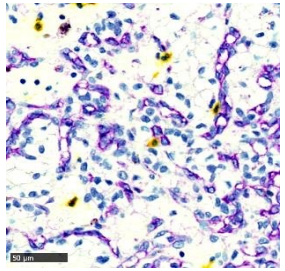
Exploratory biomarkers during Phase 1 clinical trial

EVT801 Biomarkers Strategy

1

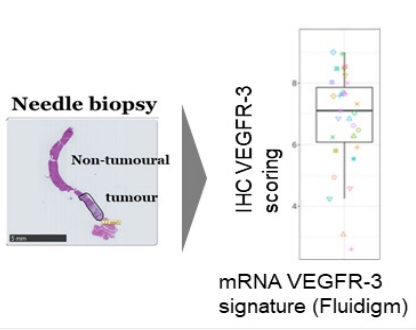
Patient characterization based on VEGFR-3 /CAIX/CD8 expression on archival tissues and/or biopsies

- VEGFR-3 protein signature by histology
  - VEGFR-3/CAIX/CD8/CD31/PD-L1



VEGFR-3 & Resistance to PD-1 mAb mRNA signatures on archival tissues and/or biopsies:

- VEGFR-3 mRNA signature by Fluigdim
- PD-1 mAb resistance mRNA signature



2

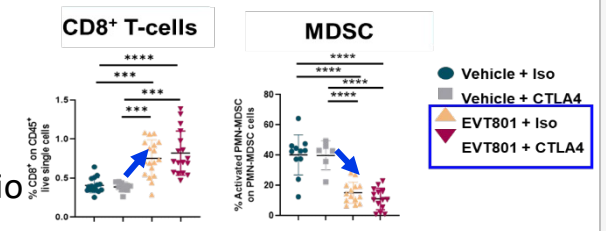
Unbiased biomarker:

- Total RNA sequencing on blood cells at C1D1 vs CD2D1

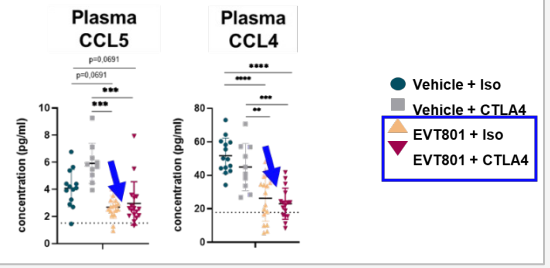
3

Circulating endpoint biomarkers:

- Immunomonitoring based on CD8^{pos} T-cells /MDSC ratio



- Proteins signature based on chemokines involved in inflammation & angiogenesis



4

Safety biomarkers to control hypertension:

- Blood pressure measurement as EVT801 dose not induce hypertension in preclinical toxicology model.

5

Resting samples will include:

- Frozen plasma, frozen whole blood, frozen PBMCs

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Study status of KZA 0801-101

EVT801 Clinical Study		
Protocol Number	**Study Name**	**Study Update**
KZA 0801-101	A Phase 1, First in Human, Open Label Study to Assess the Safety, Tolerability, and Pharmacokinetics of EVT801 in Patients with Advanced Solid Tumours	Stage 1 is complete - primary and secondary endpoints achieved: • 32 patients included in the study with 26 patients treated • 6 dosing cohorts completed ranging from 50mg QD to 500mg BID • MTD identified as 500mg BID with 400mg BID being RP2D* as monotherapy • EVT801 was well tolerated across all doses with majority of toxicities being mild to moderate and transient in nature Number of patients have remained on treatment for two or more cycles with 9 reaching cycle 3 or greater (one reached cycle 9) Biomarkers have shown strong VEGFR3 expression in some indications, and we have observed encouraging clinical activity in HGS* ovarian cancer patients (strongly expressing VEGFR3) 11 patients with ovarian cancer enrolled into the study: • All failed multiple lines of previous therapy • Average age of 67 years (range: 56-76) with a median time from diagnosis of nine years • 46% had stable disease or better for at least three cycles

* RP2D = Recommended Phase 2 Dose; HGS = High grade serous

Key Points

1. Well understood mechanism (anti-angiogenesis) with unique differentiating feature (high VEGFR3 selectivity)
2. Very strong preclinical data package, with evidence of activity in multiple tumours and favourable toxicology
3. Potential for combination use with immuno-oncology therapies
4. Ongoing phase 1 clinical study demonstrating robust safety and tolerability profile to date. Clinical and biomarker data presented at AACR 2024
5. Primary and secondary objectives of the clinical study have successfully been met - MTD and RP2D identified
6. Encouraging signal of activity in HGS ovarian cancer patients as well as strong VEGFR3 biomarker expression in multiple indications

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