ASX RELEASE
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KAZIA LICENSES GLOBAL RIGHTS TO EVT801, A NOVEL, FIRST-IN-CLASS, CLINIC-READY, VEGFR3 INHIBITOR, FROM EVOTEC SE

Sydney, 19 April 2021 – Kazia Therapeutics Limited (ASX: KZA; NASDAQ: KZIA), an oncology-focused drug development company, is pleased to announce that it has entered into a worldwide exclusive licensing agreement and a master services agreement with Evotec SE (FRA: EVT), a leading European drug discovery and development company, for EVT801, a small-molecule, first-in-class oncology drug candidate. Kazia expects to launch a phase I clinical trial of EVT801 in CY2021.

Key Points

- Evotec has granted Kazia an exclusive global worldwide license to develop, manufacture, and commercialise EVT801 in all territories and indications.
- Under the terms of the agreement, Kazia will pay an immediate upfront of €1 million (AU$ 1.6 million), contingent milestones of up to €308 million (AU$ 480 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.
- Evotec is a leading drug discovery and development company, headquartered in Hamburg, Germany, and listed on the Frankfurt Stock Exchange.
- EVT801 is a small-molecule inhibitor of VEGFR3. Its primary activity is to inhibit lymphangiogenesis, the formation of new lymphatic vessels around a growing tumour. By doing so, EVT801 is expected to starve the tumour of vital nutrients and to reduce metastasis. EVT801 also has marked activity on the immune system within the tumour and may therefore enhance the activity of immuno-oncology therapies.
- Kazia and Evotec have also entered into a master services agreement, under which the two companies will collaborate closely on the further development of EVT801.
- EVT801 was originally discovered by Sanofi (NASDAQ: SNY), the largest pharmaceutical company in France and among the five largest in the world and was developed through a partnership between Sanofi and Evotec.
- Kazia expects to launch a phase I clinical trial in CY2021. The initial exploratory indications for EVT801 include renal cell carcinoma (kidney cancer), hepatocellular carcinoma (liver cancer), and soft tissue sarcoma.

Kazia CEO, Dr James Garner, commented, “We are delighted to add this tremendously exciting new compound to the Kazia pipeline. Evotec have done first-class work in the early development of EVT801, and the preclinical data package is exceptionally strong. We intend to fast track a phase I clinical trial of the drug, which we expect to commence in CY2021.”

He added, “As we have built Kazia over the past five years, our strategy has been to assemble a portfolio of world-class development candidates through in-licensing. The EVT801 transaction is wholly consistent with that strategy. We have demonstrated, through the paxalisib program, our ability to add value to a development candidate, and we intend to similarly accelerate EVT801 via a rich and innovative development program.”

Evotec CEO, Dr Werner Lanthaler, commented, “we are very pleased to partner with Kazia for this promising asset, for which we have high hopes. Our corporate strategy does not provide for Evotec to take EVT801 through clinical trials itself, so we have sought to identify a partner who can do justice to the drug’s potential. We recognise Kazia’s track record and look forward to working together to make EVT801 available to patients and clinicians.”

EVT801

EVT801 is a small molecule inhibitor of vascular endothelial growth factor receptor 3 (VEGFR3). It is orally available, and so can be administered to patients by mouth.

For more than two decades, one of the most successful approaches in the treatment of cancer has been to target angiogenesis, the formation of new blood vessels. Drugs which inhibit angiogenesis, such as Avastin® (bevacizumab), starve the growing tumour of nutrients. However, inhibiting angiogenesis also results in hypoxia (low levels of oxygen) around the tumour, and this is thought to generate resistance to treatment. Almost all cancers treated with current anti-angiogenic drugs will eventually develop resistance.

An alternative approach, which may avoid this problem, is to target lymphangiogenesis, which is the formation of new lymphatic vessels. Doing so achieves many of the same objectives as targeting angiogenesis but may avoid the problem of resistance induced by hypoxia. Moreover, the lymphatic system is a common route by which tumours spread (metastasise) throughout the body, and so inhibiting lymphangiogenesis may help to limit the ability of the tumour to spread.

In recent years, several new drug candidates have attempted to inhibit lymphangiogenesis. For example, Nexavar® (sorafenib) inhibits several forms of VEGFR, as well as other targets, and is approved for the treatment of renal cell carcinoma and hepatocellular carcinoma. Several drugs described as angiokinase inhibitors are in development, and some of these inhibit VEGFR3. However, each of these drugs has multiple targets, leading in many cases to significant side effects. The distinguishing feature of EVT801 is a high degree of specificity for VEGFR3, which should allow it to minimise toxicity.

In addition, EVT801 has shown powerful evidence in the laboratory of an ability to change the balance of immune cells within the tumour. Many tumours are resistant to the newest

generation of immuno-oncology therapies because they do not contain the right immune cells for the drugs to act upon. It is hoped that administration of EVT801 may help to sensitise these tumours to immuno-oncology therapies such as Keytruda® (pembrolizumab) and Opdivo® (nivolumab) and thereby extend their use.

Kazia expects to explore all these potential uses of EVT801 during the clinical program. The initial focus will be on a phase I study, which is expected to be conducted at one or more leading hospitals in France and to commence in CY2021.

Master Services Agreement

In parallel with the license agreement, Kazia and Evotec have entered into a Master Services Agreement (MSA), under which they will collaborate on the further development of EVT801. Kazia intends to utilise Evotec's substantial capabilities and expertise in research, clinical trial management, biomarker development, and manufacturing, to expedite the development of EVT801.

Investor Conference Call

Kazia is pleased to invite investors to attend a conference call to further discuss the EVT801 in-licensing.

The call will be held on Tuesday 20 April 2021 at 8:00am, Sydney time (AET), which is 6pm on Monday 19 April in New York (ET) and 3pm on Monday 19 April in San Francisco (PT).

Participants will need to **pre-register** for the call via the following link:

Registration Link: https://s1.c-conf.com/diamondpass/10013602-bric5f.html

Click the 'Register Now' button and follow the prompts to complete pre-registration. You will then receive a calendar invite with dial in numbers, a passcode and a PIN to dial into the conference call.

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About Kazia Therapeutics Limited

Kazia Therapeutics Limited (NASDAQ: KZIA; ASX: KZA) is an oncology-focused drug development company, based in Sydney, Australia.

Our lead program is paxalisib, a brain-penetrant inhibitor of the PI3K / Akt / mTOR pathway, which is being developed to treat glioblastoma, the most common and most aggressive form of primary brain cancer in adults. Licensed from Genentech in late 2016, paxalisib commenced recruitment to GBM AGILE, a pivotal study in glioblastoma, in January 2021. Seven additional studies are active in other forms of brain cancer. Paxalisib was granted Orphan Drug Designation for glioblastoma by the US FDA in February 2018, and Fast Track Designation for glioblastoma by the US FDA in August 2020. In addition, paxalisib was granted Rare Pediatric Disease Designation and Orphan Designation by the US 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. Preclinical data has shown EVT801 to be active against a broad range of tumour types and has provided compelling evidence of synergy with immuno-onocology agents. A phase I study is expected to begin in CY2021.

For more information, please visit www.kaziatherapeutics.com or follow us on Twitter @KaziaTx.

About Evotec SE

Evotec is a drug discovery alliance and development partnership company focused on rapidly progressing innovative product approaches with leading pharmaceutical and biotechnology companies, academics, patient advocacy groups and venture capitalists.

We operate worldwide and our more than 3,500 employees provide the highest quality stand-alone and integrated drug discovery and development solutions. We cover all activities from target-to-clinic to meet the industry's need for innovation and efficiency in drug discovery and development (EVT Execute). The Company has established a unique position by assembling top-class scientific experts and integrating state-of-the-art technologies as well as substantial experience and expertise in key therapeutic areas including neuronal diseases, diabetes and complications of diabetes, pain and inflammation, oncology, infectious diseases, respiratory diseases, fibrosis, rare diseases and women's health.

On this basis, Evotec has built a broad and deep pipeline of more than 100 co-owned product opportunities at clinical, pre-clinical and discovery stages (EVT Innovate). Evotec has established multiple long-term alliances with partners including Bayer, Boehringer Ingelheim, Bristol Myers Squibb, CHDI, Novartis, Novo Nordisk, Pfizer, Sanofi, Takeda, UCB and others. For additional information please go to www.evotec.com and follow us on Twitter @Evotec.

This document was authorized for release to the ASX by James Garner, Chief Executive Officer, Managing Director.

Q&A

What has attracted Kazia to the EVT801 asset?

Like paxalisib, EVT801 provides a comparatively well-understood mechanism of action but is also uniquely differentiated from other drug candidates in its class. The drug targets angiogenesis, which is a very well-validated approach to the treatment of cancer. However, due to its specificity for VEGFR3, EVT801 has a much greater effect on the development of lymphatic vessels than on blood vessels, and this specificity sets it apart from other anti-angiogenic drugs.

At a more practical level, EVT801 has been the subject of extensive preclinical testing by Evotec, which has yielded a first-class data package. There is detailed confirmation of the drug's mechanism, clear proof of activity in multiple tumour types, exciting combination data with immunotherapy agents, and an impressive battery of animal toxicology data that shows the drug to be safe and tolerable on present evidence.

What other VEGFR3 inhibitors are on market or in development, and how will EVT801 be differentiated?

Kazia is not aware of other agents that match the specificity of EVT801. Several approved products have demonstrated or potential activity against VEGFR3 among a range of other biochemical targets, including:-

Drug	Manufacturer	Targets
Nexavar® (sorafenib)	Bayer	VEGFR, PDGFR, RAF kinases
Sutent® (sunitinib)	Pfizer	VEGFR, PDGFR
Votrient® (pazopanib)	Novartis	VEGFR, PDGFR, c-Kit, FGFR
Inlyta® (axitinib)	Pfizer	VEGFR, c-Kit, PDGFR
Ofev® (nintedanib)	Boehringer-Ingelheim	VEGFR, FGFR, PDGFR

There are several potential advantages to a VEGFR3-specific agent such as EVT801. The primary advantage is expected to lie in a more favourable toxicity profile. Other drugs in the angiokinase inhibitor class are typically associated with significant toxicity, and this often limits their use in clinical practice. The majority of these toxicities are believed to be unrelated to their activity against VEGFR3. A selective VEGFR3 inhibitor is expected to be substantially more tolerable for patients, enabling a longer duration of treatment to a broader group of patients, with greater potential for combination therapy.

A secondary advantage of EVT801's specificity is that its main mechanism of action is expected to reside in the inhibition of lymphangiogenesis (formation of new lymphatic vessels) more than the inhibition of angiogenesis (formation of new blood vessels). While the therapeutic benefits of the two approaches may be similar, inhibition of lymphangiogeneiss is hypothesized to be less prone to development of treatment

resistance. As such, EVT801 may substantially avoid the issues of drug resistance that have constrained many other therapies in this class.

What tumour types will EVT801 be developed for? Will you be testing the drug in brain cancers?

Kazia will initially focus on tumours which are known to express VEGFR3 to a high degree, and / or which are known to be highly dependent on lymphangiogenesis. These tumours include renal cell carcinoma (kidney cancer), hepatocellular carcinoma (liver cancer), soft-tissue sarcoma, and others. However, it is possible and indeed likely that other tumour types will be explored during the development of EVT801.

Kazia has no current plans to develop EVT801 for brain cancer, but this may be revisited in the light of emerging data.

Will EVT801 be tested in combination with paxalisib?

Kazia has no current plans to trial EVT801 in combination with paxalisib. Scientifically, there is a limited rationale for that specific combination. Strategically, Kazia intends to keep the programs independent, such that neither relies on the success of the other.

What is the market opportunity for EVT801?

The market opportunity for a drug at this stage of development is difficult to quantify. Existing angiokinase inhibitor drugs typically report annual sales of approximately US$ 1 billion on average. However, that generalization disguises the fact that these agents are approved for quite different patient populations, and the class contains a mixture of very mature products and more recent additions. For example, Sutent® (sunitinib) was first approved in 2006, while Votrient® (pazopanib) was first approved in 2012.

Technavio, a global market research and consulting company, forecasts the VEGFR inhibitor market to reach US$ 10.2 billion in annual sales by 2023, with annual growth of 8%.[1]

Considered from a different angle, Grand View Research forecasts the market opportunity associated with renal cell carcinoma to exceed US$ 6 billion in annual sales by 2022,[2] and the market opportunity for hepatocellular carcinoma to reach annual sales of approximately US$ 1.5 billion in the same period.[3]

What is the scope of the master services agreement between Kazia and Evotec?

[1] https://www.technavio.com/report/vascular-endothelial-growth-factor-vegf-inhibitors-market-industry-analysis
[2] https://www.grandviewresearch.com/press-release/global-kidney-cancer-drugs-market
[3] https://www.grandviewresearch.com/press-release/global-liver-cancer-drugs-market

Kazia and Evotec have entered into a master services agreement (MSA), concurrent with the license agreement for EVT801. The MSA is broad in scope and provides for Kazia to utilize Evotec's services across preclinical validation, manufacturing, formulation development, biomarker development, and in other areas.

Any services provided by Evotec under the MSA will be on commercial terms, and both companies retain customary ability to terminate the MSA at any time without affecting the license agreement for EVT801. Kazia is free to work with other business partners at its sole discretion for any aspect of the development and commercialization of EVT801.

Does Evotec retain a call option or right of first refusal to re-acquire EVT801 in the future?

No. Kazia retains an unrestrained right to partner EVT801 to one or more companies of its choice.

Aside from Evotec, will Kazia have any commitments to third parties arising from this transaction?

No. Aside from customary legal and transactional expenses, there are no participatory economics involving third parties. Evotec is subject to undisclosed financial commitments to Sanofi, under a 2015 license agreement between those companies, but those obligations are not expected to result in any additional commitments for Kazia.

What is planned for the phase I trial of EVT801?

Kazia expects to launch a phase I, first-in-human study of EVT801 by the end of CY2021.

As is typical for investigational new drugs such as EVT801, this first study will be focused on understanding the safety and tolerability of the drug, and on determining the maximum tolerated dose (MTD) for future investigation. The study is also expected to include a detailed exploration of biomarkers and other mechanistic assessments.

Kazia and Evotec are in advanced discussions to conduct the study at two centres in France. Kazia expects to disclose more information about the phase I study during Q3 CY2021.

What is the strategic rationale behind licensing another asset?

Kazia's corporate strategy has always envisaged the in-licensing of multiple promising drug development candidates. Having a diversified pipeline mitigates risk, by avoiding dependence on a single asset, and allows for the company to achieve critical mass, developing infrastructure for the pipeline that would not be cost-effective for a single asset. The EVT801 transaction is wholly consistent with this strategy.

Does this transaction represent any strategic shift away from paxalisib or from brain cancer?

No. Paxalisib remains Kazia's lead program and the company continues to be wholly committed to its development and commercialization. In Q1 CY2021, Kazia announced the initiation of recruitment to the paxalisib arm of the GBM AGILE pivotal study, and also announced a partnering transaction with Simcere Pharmaceutical for Greater China rights to the asset, in a deal worth up to US$ 292 million plus royalties.

How will Kazia fund the development of EVT801?

Kazia expects to cover immediate expenses associated with EVT801 from recent licensing revenues.