Biotech Daily

Friday June 10, 2022

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH DOWN: PRESCIENT UP 6%; AMPLIA DOWN 12%**

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MARKET REPORT

The Australian stock market fell 1.25 percent on Friday June 10, 2022, with the ASX200 down 87.7 points to 6,932.0 points.

Eight of the Biotech Daily Top 40 stocks were up, 24 fell, seven traded unchanged and one was untraded.

Prescient was the best, up one cent or 5.6 percent to 19 cents, with 3.3 million shares traded. Volpara was up 3.45 percent; Compumedics and Cynata rose more than two percent; Immutep and Pharmaxis were up more than one percent; with Avita, Pro Medicus and Resmed up by less than one percent.

Amplia led the falls, down 1.5 cents or 12.0 percent to 11 cents, with 520,076 shares traded, followed by Alcidion down 1.5 cents or 11.5 percent to 11.5 cents, with 4.25 million shares traded.

Starpharma and Universal Biosensors lost more than seven percent; Dimerix, Medical Developments, Micro-X and Proteomics retreated more than six percent; Atomo, Opthea and Uscom were down more than five percent; Impedimed and Orthocell fell four percent or more; Oncosil was down 3.85 percent; Nanosonics and Neuren shed more than two percent; Antisense, Genetic Signatures and Kazia were down one percent or more; with Clinuvel, Cochlear, CSL, Emvision, Next Science, Polynovo and Telix down by less than one percent.

DR BOREHAM'S CRUCIBLE: KAZIA THERAPEUTICS

By TIM BOREHAM

ASX code: KZA; **Nasdaq code:** KZIA (One Nasdaq American depositary share to 10 ASX shares)

Share price: 78 cents; **Shares on issue:** 133,912,566; **Market cap:** $104.5 million

Chief executive officer: Dr James Garner

Board: Iain Ross (chair), Bryce Carmine, Steven Coffey, Dr Garner

Financials (March quarter 2021): revenue nil, cash outflows $6.53 million, cash on hand $6.95 million, quarters of available funding 1.06 (see below).

Major identifiable holders: Willoughby Capital 14.6%, Quest Asset Partners 8.4%, Platinum Asset Managers 5.4%.

In the race to get a therapy to market, drug developers usually keep a wary eye on potential rivals and hide their intellectual property well out of sight.

But in the case of brain cancer drug developer Kazia, there's more merit in 'co-opetition' and consorting with one's 'frenemies'.

Unusually, Kazia is conducting a phase III trial of its glioblastoma drug paxalisib via a collective program called GBM Agile (GBM is shorthand for the glioblastoma).

Formerly known as GDC-0084, paxalisib tackles the glioblastoma multiforme variant which accounts for about 15 percent of all brain cancers.

Paxalisib aside, four other drugs are being trialled via the GBM Agile platform, which is independent of any particular company.

"The drug seems to be extending the life of patients with glioblastoma, which is a big deal because not much else does," says Kazia chief Dr James Garner.

While glioblastoma remains the flagship indication for paxalisib and is by far the most advanced, Kazia has five other clinical studies underway and has in-licenced an unrelated cancer drug candidate.

The company has also executed three cross-border licencing deals.

Ancient history

Kazia was formerly known as Novogen, Australia's second-oldest listed biotech behind Circadian (now Opthea). Novogen bought glioblastoma candidate GDC-0084 from Glioblast Pty Ltd, which had earlier licenced the compound from Roche's Genentech.

Glioblast was owned by biotech Hall of Famer Paul Hopper and Imugene chief executive Leslie Chong, who oversaw development of GDC-0084 while at Genentech.

Founded by Dr Graham Kelly, Novogen listed on the ASX in 1994 and then on the US Nasdaq in 1998.

After the company dabbled unsuccessfully in pursuits including red clover leaf derivatives, veterinary products and women's natural health supplements, Dr Garner was recruited in 2016 to imbue a more commercial focus.

In 2017, Novogen changed its name to Kazia - a confected Hebrew-sounding name that has nothing to do with khazis … unless of course its programs go down the toilet.

Modern history

In February 2018, paxalisib won 'orphan drug' status from the US Food and Drug Administration (FDA), with fast-track designation awarded in 2020.

In 2020, Kazia also picked up FDA rare paediatric disease designation for a rare and aggressive childhood brain cancer, called diffuse intrinsic pontine glioma (DIPG). And for those who missed it, DIPG Awareness Day was on May 17.

In March 2021, Simcere Pharmaceutical agreed to take up the greater China rights to paxalisib, for $US11 million upfront and up to $US292 million in royalties.

Also in March, Kazia hived off its legacy ovarian cancer drug candidate, Cantrixil. The deal involved a $US4 million upfront payment and $US42 million of potential milestone payments.

In April 2021, Kazia then in-licenced EVT801, a small molecule inhibitor of the vascular endothelial growth factor receptor-3 (VEGFR3) antibody, from German group Evotec SE. The terms were EUR1 million ($A1.5 million) upfront and EUR300 million of potential royalties and milestones.

How it works

While glioblastoma has claimed high-profile victims including former US presidential candidate John McCain and Joe Biden's son Beau, there's been little progress in treating the disease.

The main treatment is temozolomide, marketed by Merck as Temodar before it went off patent. The drug is considered effective in about one-third of cases.

Paxalisib inhibits a signalling pathway called PI3K, which is expressed in 85 percent to 90 percent of glioblastoma tumors. While this inhibitor class is well established, Kazia claims that paxalisib can cross the blood-brain barrier, the membrane that keeps foreign agents out of the grey matter.

Overall, more than 150 patients have been treated with paxalisib.

In December 2021 the company released final “broadly positive” results of a 30-patient, phase II study, confirming earlier work showing a five months’ median extension in overall survival to 17.7 months, compared with 2.7 months for the control group on temozolomide. Progression free survival time (that is, the tumor not spreading) was extended from 5.3 months to 8.4 months.

Hands across the water

Buoyed by the interim analysis, in January last year, Kazia launched the phase III study via GBM Agile. It’s expected that about 200 patients will be treated with paxalisib, with a similar-sized control group treated with temozolomide.

As measured by overall survival, positive results could lead directly to an FDA marketing application.

In November last year, the trial opened at the Sunnybrook Health Sciences Centre in Toronto, Canada. Late last month, the first European paxalisib arm opened, in Switzerland, which adds to 40-plus US and Canadian sites.

Dr Garner says while multiple drug ‘platform’ trials are new, the FDA has been championing the idea for some years.

“The approach offers the benefit of standardization - similar data for each drug - which makes the regulator’s job easier,” he says. “The machinery of the trials is set up only once and the trial sites sign only one contract to be involved in multiple studies.”

To avoid conscious or unconscious bias, the drug candidates are allocated to patients centrally and randomly.

Dr Garner says that because of efficiencies such as a shared control arm, the cost of the trial to Kazia is about one-third of what it would have been on a stand-alone basis. Final data is expected in 2023.

Another time and cost saving feature of GBM Agile is that it’s adaptive: patients numbers can be adjusted as results emerge.

Giving kids a chance

Chemotherapy is the only treatment option for kids with DIPG and life expectancy is only nine to 10 months.

The company has completed a phase I safety and dosing study at St Jude Children’s Research Hospital in the US. A quasi-phase II study has kicked off in collaboration with the Pacific Pediatric Neuro-oncology Consortium (PNOC).

Because a new drug is likely to do better and certainly no worse than chemo, Dr Garner says the approval bar is not high and even modest data could sway the FDA.

The FDA has also awarded the company was a paediatric priority review voucher, a Willy Wonka style ticket that enables fast-track FDA assessment of a new drug application. The quirk of the scheme is that the value of the voucher is crystallised by FDA approval of the children's treatment, in this case for DIPG.

The idea is the holder uses the voucher for a second drug, or more likely, sells the right to another drug company. The vouchers have sold for as much as $US350 million.

"Glioblastoma remains lead indication, but some of these childhood cancers are rapidly emerging as really important second strings," Dr Garner says.

Angiogenesis and all that

EVT801 combines the new art of immune-oncology with the old one of angiogenesis.

For the uninitiated - and don't be embarrassed - angiogenesis is the physiological process through which new blood vessels form from pre-existing vessels.

EVT801 was invented by drug giant Sanofi, with most pre-clinical work done by European contract research organization Evotec. Kazia in-licenced the drug in April and started a phase I trial in November, in France.

Early work suggests the inhibitor is effective against a broad range of tumors, as a monotherapy or in combination with immune-oncology agents.

Also bubbling away …

Boston's Dana-Farber Cancer Institute is carrying out a phase II trial to test paxalisib on primary central nervous system (CNS) lymphoma. Initial data is expected later this year.

Kazia also has three on-going trials in brain metastases: cancers spread from elsewhere in the body (most often lung, breast and melanoma). There are about 200,000 brain metastases in the US a year, compared with 12,500-13,000 for glioblastoma, 2,000 for primary CNS lymphoma and a mere 500 for DIPG.

"There are a lot of ways we can use this drug in a range of different patients," Dr Garner says.

Finances and performance

As of December 2021, Kazia had $15.2 million in the bank, having burnt $4.27 million during the quarter.

Dr Garner says while it's hard to be definitive, the company has enough dosh for the time being. In April it opened an at-the-market (ATM) facility with a $US35 million cap. ATMs enable companies to place shares directly to investors in an effective way, usually in smaller tranches.

Beyond that, the company expects more milestones payments and grant funding, both here and in the US.

"We have quite a few levers to move," Dr Garner says. "We may end-up needing a bit more money before we get to the finish line, but that can come from beyond a capital raising."

The company last went to the well in October 2020, raising $24 million with the backing of investors including Platinum Asset Management and Quest Asset Partners.

Kazia shares have been affected by the sector's horror patch, losing 40 percent of their value so far this calendar year. About 80 percent of Kazia's stock is traded on the Nasdaq.

Kazia shares peaked at $1.88 in early April last year and then hit a low of 71 cents on May 13 this year.

Dr Boreham's diagnosis:

When we last covered Kazia, in September 2020, Dr Garner said the company had reached an "endgame" where management starts to focus on commercialization rather than drug exploration.

Kazia does appear to have reached an inflexion point.

As the company's 2021 annual report says: "in subtle but fundamental ways the game has changed".

The glioblastoma program is promising because the disease is rare, but not too rare. In other words, the market is small enough for most drug developers to ignore, but big enough to be quite lucrative.

Temodar (temozolomide) was a $US1 billion-a-year earner for Merck before the drug went off patent.

There will always be debate about the merits of a drug that adds two to three months to a patient's life expectancy.

As usual, we're not talking about a cure. But Dr Garner says a 25 to 33 percent life extension is material and better than that achieved by other approved cancer drugs.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. In subtle but fundamental ways, that is important.

TELIX PHARMACEUTICALS

Telix says it will expand its partnership with the Hayward, California-based Reflexion Medical, developing Illuccix as the biological guide for Reflexion's radiotherapy.

In 2020, Telix said it would collaborate with Reflexion to evaluate the potential for its positron emission tomography (PET) tracers, and Illuccix, formerly 61-gallium-prostate-specific membrane antigen-11 (68Ga-PSMA-11) to guide Reflexion's radiotherapy platform in prostate and kidney cancer (BD: Jul 8, 2020).

Today, the company said that under the agreement, the two companies would co-fund a clinical program for Reflexion's biology-guided radiotherapy, exclusively using Illuccix as the platform's biological guide.

Telix said that the biology-guided radiotherapy used PET tracers as biological guides to signal the location of cancer and guide the delivery of radiotherapy to tumors in real-time.

The company said the method had "the potential to offer significant advantages over conventional radiotherapy as it may one day enable treatment of multiple tumors per session for metastatic disease, increase the conformality of radiotherapy delivery and reduce toxicity to healthy tissue".

Telix said that biology-guided radiotherapy might facilitate treatment of later stage cancers than was currently practical for hospitals or tolerable by patients.

The company said the partnership would seek regulatory approval and jointly pursue commercialization in the US initially, sharing revenues if commercialization was successful.

Telix chief executive officer Dr. Christian Behrenbruch said the company was "pleased to expand our relationship with Reflexion and move ahead with a clinical program with the objective of regulatory approval of Illuccix for [biology-guided radiotherapy]".

"This partnership demonstrates the potential for Illuccix and other molecularly-targeted imaging agents in our pipeline to be used as a tool to both detect the presence of metastatic disease and guide treatment using innovative complementary technologies such as [biology-guided radiotherapy]," Dr Behrenbruch said.

Telix fell three cents or 0.7 percent to $4.03 with 799,473 shares traded.

CHIMERIC THERAPEUTICS

Chimeric says it has completed manufacture and quality release of a viral vector for its CHM1101 chlorotoxin chimeric antigen receptor T-cell solid tumor treatment.

In February, Chimeric said it had "encouraging initial data" for the second cohort in its chlorotoxin chimeric antigen receptor T-cells (CLTX-Car-T-cells) phase I dose escalation study (BD: Feb 8, 2022).

Today, the company said the viral vector was developed and manufactured at the Duarte, California-based City of Hope.

Chimeric said that developing a viral vector was "one of the most challenging and critical components of cell therapy technical operations", with vectors key to the manufacture of a Car-T-cell therapies like CHM1101.

The company said a shortage of vector manufacturing capacity had "significantly delayed other cell therapy company development programs, as well as challenging commercial manufacturers", making its development of a vector "a critical milestone".

Chimeric managing-director Jennifer Chow said the manufacture of the viral vector "marks a major milestone for advancing the development of CHM1101".

"Vector supply significantly challenges the cell therapy industry with current backlogs of more than a year to access vector manufacturing," Ms Chow said.

Chimeric was unchanged at 10.5 cents.

BTC HEALTH

The Sydney-based LHC capital says it has reduced its substantial holding of BTC, from 22,500,000 shares (9.14%) to 22,319,290 shares (7.92%).
In a substantial shareholder notice signed by LHC chief executive officer Stephen Aboud, the company said that on June 7, 2022, it sold 240,000 BTC shares, but did not specify the consideration given, as required under the Corporations Act 2001.
Last year, BTC said it had raised $2.5 million at seven cents a share, issuing 35,714286 shares (BD: Jul 2, 2022).
BTC was untraded at four cents.

REGENEUS

Regeneus says chief executive officer Karolis Rosickas has bought 3,836,366 shares off market for $153,455 or four cents a share.
Mr Rosickas said he had “a firm conviction in the value of Regeneus’ differentiated technology and its clinical pipeline”.
“Cell and gene therapies are becoming a more prominent modality in the pharmaceuticals industry and Regeneus is at the forefront in developing and commercializing novel and highly efficacious treatments for patients,” Mr Rosickas said.
Regeneus fell 0.1 cents or two percent to 4.9 cents.

MTP CONNECT
COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANISATION

MTP Connect says the Commonwealth Scientific and Industrial Research Organisation has provided a further $1 million for the Redi program.
MTP Connect chief executive officer Stuart Dignam said that the Researcher Exchange and Development within Industry (Redi) Fellowship program had reopened to provide grants of up to $250,000.
Mr Dignam said that the program was funded by the Medical Research Future Fund and operated by MTP Connect, providing industry “the opportunity to select a researcher, academic, clinician or technology transfer professional to collaborate on priority medical research projects involving discovery, translation, and commercialization”.
Mr Dignam said 32 Redi fellows had worked with CSL, Cochlear, Telix, Leica Biosystems, Stryker, Speedx, Paige AI, Pharmaxis and Synopsys.
“The Redi Fellowship program has been an outstanding success,” Mr Dignam said.
“Not only do fellows benefit from working in industry, but when they return to their home institution after their placement, they share their industry experiences within the research sector and contribute to a commercialization-focused culture change,” Mr Dignam said.
MTP Connect said that eligible companies and organizations needed to submit an application identifying a fellow and match it with a specific research and development project, with applications closing on July 27, 2022.
For more information about the Redi program and to apply, go to: https://www.mtpconnect.org.au/Category?Action=View&Category_id=293.