Biotech Daily

Friday September 15, 2023

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH UP: VOLPARA UP 8%; ACTINOGEN DOWN 9%**

*** DR BOREHAM'S CRUCIBLE: CLARITY PHARMACEUTICALS**

*** MEMPHASYS INDIA STUDY: 11 LIVE IVF FELIX BIRTHS**

*** NEUROTECH APPOINTS MERCHANT ADVISOR; 25m OPTIONS**

*** PERENNIAL REDUCES TO 14% IN GENETIC SIGNATURES**

*** COCHLEAR UP-TO $2.5m CEO DIG HOWITT LONG-TERM INCENTIVES AGM**

MARKET REPORT

The Australian stock market was up 1.29 percent on Friday September 15, 2023 with the ASX200 up 92.5 points to 7,279.0 points.

Eighteen of the Biotech Daily Top 40 stocks were up, 15 fell, three traded unchanged and four were untraded.

Volpara was the best, up 5.5 cents or 7.9 percent to 75 cents, with 85,147 shares traded.

Immutep and Patrys climbed six percent or more; Atomo, Nova Eye, Polynovo and Telix improved more than five percent; 4D Medical was up 4.7 percent; Antisense, Avita and Cynata were up three percent or more; Mesoblast rose 2.4 percent; Emvision, Nanosonics, Pharmaxis, Pro Medicus and Resonance were up more than one percent; with CSL, Prescient and Resmed up by less than one percent.

Actinogen led the falls, down 0.2 cents or 9.1 percent to two cents, with 5.1 million shares traded.

Paradigm and Starpharma lost more than six percent; Next Science was down 5.4 percent; both Alcidion and Micro-X fell 4.35 percent; Cyclopharm was down 3.8 percent; Compumedics, Genetic Signatures and Neuren shed more than two percent; Dimerix, Opthea and Orthocell were down more than one percent; with Clinuvel, Cochlear and Medical Developments down by less than one percent.

DR BOREHAM'S CRUCIBLE: CLARITY PHARMACEUTICALS

By TIM BOREHAM

ASX code: CU6

Share price: $1.24

Shares on issue: 261,859,233

Market cap: $324.7 million

Financials (year to June 30 2023): revenue nil, loss of $24.6 million (previous $23.8 million deficit), cash balance $65 million (down 29%).

Chief executive officer: Dr Colin Biggin

Board: Dr Alan Taylor (executive chair), Dr Biggin, Dr Chris Roberts, Dr Thomas Ramdahl, Rosanne Robinson, Rob Thomas, Cheryl Maley

Identifiable major shareholders: TM Ventures Pty Ltd 7.2%, Cabbit Pty Ltd 6.8%, Taylor Family 5.1%, Charles Morgan 2.7%, Boorriss Pty Ltd (Matt Harris) 2.3%.

The radiopharmaceuticals outfit's market valuation has been irradiated since it raised a record $92 million and listed just over two years ago. Meanwhile, its bigger and wildly successful peer Telix Pharmaceuticals hogs the investor limelight.

But Clarity executive chair Dr Alan Taylor is unfazed about feeling like a fifth Wiggle or the fifth Beatle, as Clarity pursues diagnostic and therapeutic applications on several fronts.

"We have achieved the milestones we set out to achieve and some of them are going faster than we thought," Dr Taylor says, adding the market conditions have made for a "wild ride".

A quiet toiler, Clarity is pursuing a full clinical slate covering diagnostic and therapeutic applications for its copper isotopes, including prostate cancer, breast cancer and children's neuroblastoma.

In gruesome marketing speak, this two-way pursuit is known as 'theranostics'.

Isotopes, by the way, are derivatives of an element on the periodic table that share the same number of protons but have a different number of neutrons. But we all knew that, didn't we?

While nuclear medicine is nothing new, Dr Taylor says targeted radiopharmaceuticals is a relatively new area, with some "great science" emerging.

Including Clarity's of course.

Here's some Clarity

Clarity was formed in 2010, based on the work of also the late Dr Alan Sargeson at the Australian National University and Prof Paul Donnelly at the University of Melbourne's Bio21 Institute of Molecular Science and Technology, with a little help from the Australian Nuclear Science and Technology Organisation (ANSTO).

Clarity is based in Sydney's gentrified, inner-city Redfern and has subsidiaries in Belgium and the US.

The technology is based around its SAR (short for Sarcophageal) platform and two radioisotopes: copper-64 and copper-67. The former isotope is for improved PET (positron emission tomography) scanning and the latter is for actual therapy.

Cat-chelator, patients

Clarity uses a functional 'cage' called a chelator, which prevents the leakage of copper into the body. The cage is linked to a targeting molecule, which finds and binds specific receptor cancer cells.

With a half-life of 12.7 hours, copper-64 can enable imaging over a longer period, which is more effective at detecting tumors. Patients can be administered and imaged the next day. Unlike the commonly used gallium - which has a half-life of only one hour - copper-64 can be made at a central facility and then transported to where it is needed.

In June Clarity said it had established a centre of excellent for copper diagnostics and therapy at the Idaho Accelerator Centre, which is operated by Idaho State University.

As well as furthering research and development, a key motive for Clarity was to be close to source of copper isotope production.

Speaking of which, Clarity also announced that its Wisconsin-based exclusive manufacturing partner Northstar Radioisotopes had completed large-scale production of the isotopes to be used in Clarity's trials.

One vaunted reason for the slow development of copper isotope therapies has been the difficulty in isolating high-purity quantities.

Glowing with talent

Clarity is replete with medical bigwigs with a high degree of commercial nous.

Dr Taylor trained at the Garvan Institute in Sydney but then entered investment banking and developed a passion for developing "good Australian science".

CEO Dr Colin Biggin was from Norwegian radiotherapy pioneer Algeta ASA, where he helped to commercialise Algeta's metastatic prostate cancer product, Xofigo.

Clarity board member Dr Thomas Ramdahl was the first CEO of Algeta, which was acquired by Bayer AG.

Clarity director Rosanne Robinson was ANSTO's business development chief, while Rob Thomas headed Citibank Australia.

Dr Chris Roberts needs no introduction as former Cochlear chief and - for a while -chaired the targeted radiotherapy play Oncosil, along with his earlier roles as a founding director of Resmed and a former chair of Sirtex Medical.

Propellor takes off in new direction

Clarity recently completed a local, phase II, diagnostic trial called 'Propellor' showing enhanced accuracy relative to the gallium-based standard of care.

Propellor showed the uptake of the copper agent in PSMA-expressing lesions was higher when compared to approved imaging agents in Australia and the US.

In early July the FDA agreed to a pivotal phase III trial for copper-64 as a diagnostic for high-risk participants prior to a radical prostatectomy.

One of the trial's key aims is to evaluate the clinical benefit of delayed imaging, the result of copper-64's superior half-life.

Called Clarify, the non-randomised, single arm, open-label trial is expected to enrol 383 patients, and kick off by the end of the year.

As a pivotal trial, the results could provide enough evidence for FDA approval.

Securing promising results

Called Secure, a phase I/IIa therapy dose-escalation trial is being carried out in the US.

Aimed at enrolling up to 44 patients, Secure investigates the use of both copper isotopes for metastatic castrate-resistant prostate cancer.

The copper-64 isotope is used to visualise the PSMA-expressing lesions and select candidates for subsequent copper-67 therapy

In August, the company said that three patients had received the second dose level with no dose limiting toxicities.

All patients responded with a drop in their prostate specific antigen (PSA) levels, with two of the three having a “massive” 90 percent reduction.

The therapy was compared with - and outperformed - the standard of care, the Novartis-owned Pluvicto.

“A PSA decline of 50 percent or greater is one of the primary endpoints of the Secure trial and a commonly-used surrogate endpoint for efficacy in this patient population,” the company says.

Alternative expression

What about the one-quarter of prostate cancers which don’t express PSMA, or metastatic castrate-resistant prostate cancer sufferers who are not suitable for PSMA therapy?

Glad you asked - and Clarity has it covered with three separate trials here and in the US.

In November last year, the FDA approved a phase I/IIa diagnostic and therapeutic trial called Combat. This one involves the company’s variant products called Sar-Bombesin, which is relevant for numerous cancers targeting the commonly-expressed gastrin-releasing peptide receptor - or GRPr.

These include prostate and breast cancers.

The company plans to recruit up to 38 patients.

“We envision that Sar-Bombesin will not only be used as a standalone product for diagnosing and treating prostate cancer, but also in combination with PSMA agents to identify and treat both PSMA and GRPr-expressing tumors,” Dr Taylor says.

Bop till you (hopefully don’t) drop

Then there’s a diagnostic trial called Bop.

This week Clarity said that early data from its phase II, investigator-led, BOP trial showed that 64-copper Sar-Bombesin identified eight of 25 (32.0%) of negative or equivocal standard-of-care prostate cancer patients, which was far better than the standard-of-care.

Clarity said no adverse events were reported and “64-copper Sar-Bombesin PET avid disease was identified in over 30 percent of patients with negative or equivocal standard-of-care PSMA PET”.

“This is the difference between having an incorrect negative cancer diagnosis leading to cancer progression and now having an effective treatment plan that may lead to long term remission,” Dr Taylor said.

Did someone mention Telix?

Targeting PSMA, Telix's gallium-based agent Illucix (Ga-PSMA-11) has been approved as a prostate cancer diagnostic in the US and elsewhere and is being trialled as a therapy.

Since Illucix was launched in April 2022, this diagnosis tool has recorded sales of more than $250 million.

In developing a prostate cancer therapy, Clarity claims to be ahead of Telix, which is carrying out a local phase III trial.

The companies would compete directly if they both commercialize a therapy, but for the time being Clarity sees Pluvicto as the main likely rival.

Dr Taylor says while Telix in-licenced its antibody-based product, Clarity built its products from the benchtop and generated its own data.

"We have produced a product from scratch and we are commercializing it because we think it is a best-in-class product," he says.

Other programs

Given Clarity's technology is platform-based, the company will look at new products to expand its repertoire.

On that note, the company last month announced it had licenced a "pre-targeting" technology from New York's Sloan Kettering Cancer Centre.

It's all about making the antibodies used with radiopharmaceuticals less toxic.

Dr Taylor says the problem with antibodies is that they get bigger in the body and hit objects such as bone marrow, exposing them to unwanted radiation.

Pre-targeting involves amplifying the uptake of radiopharmaceutical products in cancerous tissues, while reducing the exposure of healthy tissues to radiation because of the slow clearance of antibodies.

The process involves 'tagging' and injecting an antibody designed to target cancer cells, followed by injection of an 'chaser' compound that attaches only to the antibody tag.

The inventors of this so-called 'click chemistry' - Prof Carolyn Bertozzi, Prof Morten Meldal and Prof Karl Barry Sharpless - won the Nobel Prize for Chemistry for their efforts in 2022.

"Hopefully it means that safer antibodies can be bought to market," Dr Taylor says.

Meanwhile, Clarity is running a phase I/II dose-escalation study for children's neuroblastomas at five sites in the US, under an investigational new drug (IND) protocol.

Finances and performance

In August 2021 Clarity raised $92 million in the biggest biotech IPO in ASX history - a record that still stands. At the risk of fuelling rivalry, the raising pipped the $50 million raised by Telix in November 2017. At the end of June, Clarity retained $65 million of cash.

Dr Taylor says the board will review the company's financial position at the end of 2023, but the current cash kitty should get the company well into next year.

At the time of listing, China Grand was poised to take an 8.5 percent stake, via the exercise of 25.5 million Clarity options. China Grand is a familiar name in radiotherapy, having acquired the ASX-listed Sirtex and struck a $450 million partnering deal with Telix (yep – there's that name again). But the tie-up was subject to a licencing deal which was not finalized in the requisite time.

"China Grand are great, but we just didn't come to terms and the options expired," Dr Taylor says. A glass-half-full chap, Dr Taylor notes there has been no dilution for Clarity shareholders and Clarity retains the China rights.

Clarity stock traded at a high of $1.48 just after the IPO and bottomed at 36 cents in June 2022.

Dr Boreham's diagnosis:

If all goes well, Clarity will have two prostate cancer diagnostics products on the market by 2026 (for PSMA and non-PSMA). By that time, the favorable US reimbursement status for the existing diagnostics – known as 'pass through' - will have been wound back and that should benefit new offerings.

Broker Wilsons dubs Clarity's diagnostic and therapeutic data as "impressive" showing "potential practice-changing benefits over current radiopharmaceutical offerings".

Of course, much can go wrong, but the Telix experience shows how a relatively small Australian biotech can crack the FDA nut - at least with a diagnostic product.

Clarity cites the size of the prostate cancer imaging market at $US1 billion to $US1.5 billion, with the PSMA-targeting radiopharmaceutical therapy market up to $US10 billion.

Dr Taylor says diagnostics are "fun" for smaller companies, but he is clear where Clarity's greater ambitions lie.

"We see great opportunities to generate good revenues from a best-in-class diagnostic product," Dr Taylor says. "But the play for us is the 'theranostic' approach which is why we are pushing our therapy data along as quickly as possible."

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He has never been clear about where his greater ambitions lie, but suffice to say they fall short of being a small nuclear power.

MEMPHASYS

Memphasys says a 33-couples study of its Felix sperm separation device for in-vitro fertilization in Coimbatore, Tamil Nadu, has produced 11 successful live births.

Earlier this year, Memphasys said a study conducted at the Coimbatore Women's Hospital Centre in Tamil Nadu, India had reported the first birth of a healthy boy using the Felix system (BD: Apr 3, 2023).

Today, the company said the study used the Felix system for males with high sperm DNA fragmentation to achieve positive pregnancy outcomes.

Memphasys said the study resulted in 40 frozen embryo transfers, with a clinical pregnancy rate of 47.5 percent.

The company said that the 40 frozen embryos led to 11 live births or 27.5 percent, compared to the Australia and New Zealand benchmark of 31.3 percent live birth rate across all patients undertaking in-vitro fertilization from frozen embryo transfers.

Memphasys said that the 27.5 percent outcome "was achieved in a demanding patient demographic, where patients had undergone at least one previously unsuccessful [in-vitro fertilization] cycle and all males had high levels of sperm DNA fragmentation".

The company said the results showed "the positive impact of the Felix system".

Memphasys said the study, titled 'First Recorded Normal Live Birth after ICSI with Electrophoretically Isolated Spermatozoa Using the Felix System' was presented by lead study clinician Dr Ramaya Jayram at the Congress of the Asia Pacific Initiative on Reproduction in Adelaide on September 9, 2023.

Dr Jayram said "the use of the Felix device enabled the patients to undertake this gentle treatment without needing to resort to invasive procedures such as surgical sperm retrieval".

Memphasys said that India was "one of the top five addressable markets globally for the Felix system" but it had to suspend sales of Felix in India following Central Drugs Standard Control Organisation changes on August 9, 2022.

The company said that the Central Drugs Standard Control Organisation "oversees the regulation of all medical devices sold in India including human assisted reproduction clinical processes".

Memphasys said it had acted on the Organisation's changes by submitting a voluntary product registration as an initial strategy to sell non-commercial quantities in India.

The company said it was also seeking regulatory advice on exporting the Felix system to India for special test purposes until it has in-country registration which would enable unrestricted importation of the device.

Memphasys was unchanged at 1.5 cents with 3.4 million shares traded.

NEUROTECH INTERNATIONAL

Neurotech says it has appointed Merchant Corporate Advisory Australia as its corporate adviser and will issue 25,000,000 options in lieu of fees.

Neurotech said Merchant's advisory services would include investor introduction and market communication services.

The company said that subject to shareholder approval the options Would be issued and exercisable at six cents each within 12-months and that each option exercised within six months would have a free "piggy back right" attaching option at the same exercise price and expiry date.

Last year, Merchant Group said it had become a substantial shareholder in Neurotech with 36,402,227 shares or 5.01 percent (BD: Nov 4, 2022).

Neurotech was up 0.6 cents or 10.5 percent to 6.3 cents with 1.6 million shares traded.

GENETIC SIGNATURES

Perennial Value Management says it has reduced its substantial shareholding in Genetic Signatures from 21,313,482 shares (14.92%) to 19,886,686 shares (13.87%).
The Sydney-based Perennial said that between April 29, 2021 and September 13, 2023 it bought and sold shares in over 300 transactions, with the single largest sale 1,280,393 shares on July 19, 2022 for $1,254,657, or 98.0 cents a share.
Genetic Signatures fell 1.5 cents or 2.8 percent to 51.5 cents.

COCHLEAR

Cochlear's annual general meeting will vote to issue $2,545,000 in long-term incentives to chief executive officer Dig Howitt, pending performance hurdles.
Cochlear said that Mr Howitt would receive a combination of 50 percent options at an exercise price of $257.69 and 50 percent performance rights, and that the options and rights would not vest until after the 2026-'27 full year results were announced.
The company said that Mr Howitt had a fixed remuneration of $2,094,722, a target short-term incentive of $2,036,000 and a maximum long-term incentive of $2,545,000 for the year to June 30, 2024.
Cochlear said the meeting would also vote to re-elect directors Prof Bruce Robinson and Michael Daniell and adopt the remuneration report.
The meeting will be held on-line and at Cochlear Headquarters, 1 University Avenue, Macquarie University, Sydney, on October 17, 2023 at 10am (AEDT).
Cochlear fell $1.62 or 0.6 percent to $261.78 with 235,068 shares traded.