Biotech Daily

Friday February 16, 2024

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH UP: NEXT SCIENCE UP 9%; NEUREN DOWN 14%**

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*** GENETIC TECHNOLOGIES LOSES DIRECTOR NICK BURROWS**

MARKET REPORT

The Australian stock market was up 0.69 percent on Friday February 16, 2024, with the ASX200 up 52.6 points to 7,658.3 points. Twenty-one of the Biotech Daily Top 40 stocks were up, 13 fell and six traded unchanged.

Next Science was the best, up three cents or 9.2 percent to 35.5 cents, with 145,290 shares traded. Alcidion and Dimerix climbed more than six percent; Medical Developments was up 5.75 percent; Curvebeam and Imugene improved more than four percent; Impedimed and Starpharma were up more than three percent; 4D Medical, Emvision, Nova Eye, Opthea, Polynovo and Resonance rose two percent or more; Amplia, Cochlear, Cyclopharm, Genetic Signatures, Orthocell, Percheron (Antisense) and Universal Biosensors were up one percent or more; with CSL and Volpara up by less than one percent.

Neuren led the falls, down $3.27 or 14.2 percent to $19.78, with 3.5 million shares traded. Clarity lost nine percent; Pro Medicus was down 7.2 percent; Mesoblast fell five percent; Compumedics was down 3.1 percent; Actinogen, Cynata and Proteomics shed two percent or more; Immutep and Paradigm were down more than one percent; with Clinuvel, Nanosonics, Resmed and Telix down by less than one percent.

DR BOREHAM'S CRUCIBLE: CSL

By TIM BOREHAM

ASX code: CSL;

US code (over-the-counter): CSLLY

Share price: $284.00

Shares on issue: 483,093,257

Market cap: $137.2 billion

Financials (first half to December 2023): record H1 revenue $US8,053 million (up 12%), record H1 net profit $US1,920 million (up 17%), earnings before interest, tax depreciation and amortisation $US3,042 million (up 21%), dividend per share $US1.19 (up 11%), cash $1,017 million (down 34%), net debt $US11,090 million (up 4%)

Chief executive officer: Dr Paul McKenzie

Board: Dr Brian McNamee (chair), Dr McKenzie, Prof Andrew Cuthbertson, Prof Duncan Maskell, Dr Megan Clark, Bruce Brook, Caroline Hewson, Marie McDonald, Alison Watkins, Samantha Lewis

Identifiable major shareholders: Blackrock Group 5.6%, State Street 5%, Vanguard Group 4.9%.

When announcing disappointing drug trial results, most drug developers take the Bing Crosby approach of accentuating the positive, eliminating the negative and not messing with Mr In Between.

So, kudos to CSL this week for getting to the point and declaring its well-anticipated heart attack megatrial failed its primary endpoint and there were "no plans for a near-term regulatory filing".

CSL shares shrank 4.8 percent after Monday's announcement, reflecting broker estimates that a successful drug could be worth perhaps $50 per CSL share.

The next day, sellers wiped off a further 2.75 percent after CSL's robust half-year numbers, which showed an "excellent" performance from the core plasma business but substandard returns from the Seqirus influenza arm and the acquired Vifor iron and kidney heart business.

Chief executive Dr Paul McKenzie was unfazed: "CSL is in a strong position to deliver annualised double-digit earnings growth over the medium term," he cooed.

Ve haf come for your blood

CSL has expanded its scope but the business still revolves around its core Behring blood plasma arm. The company collects blood plasma - notably from centres in the US where donors are paid - and makes specialist products.

The therapies are relevant for disorders such as haemophilia, primary immune deficiencies, hereditary angio-oedema and inherited respiratory disease. CSL's leading immunoglobin products are the intravenously-delivered Privigen and the subcutaneous Hizentra

Coagulation products include Idelvion, an albumin fusion protein for haemophilia B. CSL's albumin range includes Alburx and Albuminar, used for purposed such as replacing blood loss after trauma and surgery.

Specialty products include Haegarda, an esterase inhibitor for hereditary angio-oedema (severe swelling of the face and throat) and Kcentra for urgent warfarin reversal (that is, when a patient on the blood thinning medication is bleeding to death).

CSL through the ages

CSL was founded as the Government-owned Commonwealth Serum Laboratories in 1916. CSL dosed Allied soldiers with influenza vaccines and penicillin in World War Two; and helped stave off the Spanish 'flu after the Great War.

The Hawke government privatised CSL and the company listed at $2.30 in 1994.

CSL underwent a three-for-one share split in 2007, so today's shares would be worth about $870 - a 3,760 per cent gain since listing.

Formerly known as Bio-CSL, the Seqirus division makes influenza vaccines.

On listing, CSL was steered by CEO Dr Brian McNamee, who ceded to Paul Perreault in August 2013. Dr McNamee then returned as chair.

Mr Perreault stepped in March last year and was succeeded by Dr McKenzie, formerly the company's chief operating officer.

In its most transformative deal to date, in 2004 CSL acquired German plasma rival Aventis Behring. Five years later, the company tried to take over major rival Talecris Biotherapeutics, but the US competition regulator said 'no bloody way'.

The Seqirus business was engorged by the 2015 purchase of Novartis's 'flu drug arm.

In late 2021, the company paid $17 billion for the Swiss based, publicly-listed Vifor Pharma Group a global leader in nephrology and iron deficiency.

With a $140 billion market cap, CSL is the second biggest ASX-listed company behind the Commonwealth Bank and for a period was the biggest.

Finances and performance

CSL posted a 12 percent revenue surge to a record half year $US8,050 million ($A12,333 million), with net profit perking up 17 percent to $US1,920 million ($A2,940) - another half year record.

The bottom line was attributable partly to the cost of blood collections ‘trending down’ (see below). This helped the company to bolster its gross profit margin to 55.8 percent, with the aim of restoring it to the pre Covid level of 57 percent.

The powerhouse Behring plasma arm posted revenue of $US5,238 million, up 14 percent. This was on the back of immunoglobulin product revenue of $US2,757 million, up 23 percent with strong sales across all geographies.

Sales of Hizentra, the “clear market leader” in subcutaneous immunoglobulin products, gained 18 percent. Ditto, sales in haemophilia market leader Idelvion gained seven percent. CSL also has “successfully” launched Hemgenix - the world’s first haemophilia gene therapy - in the US.

Meanwhile, Seqirus increased revenue by a less impressive two percent to $US1,804 million, with growth tempered by factors including falling vaccination rates.

Low demand has resulted in an oversupply of ’flu vaccines, leading to providers discounting the doses to move stockpiles before they have to throw them out.

Broker Wilsons opines Seqirus looks to have missed an opportunity with its new quadrivalent vaccine Flucelvax “costing them market share and margin”.

Over the last year, CSL shares have traded between $308 (mid-June last year) and a low of $232 (late October). They peaked at $336 in February 2020.

Shareholder frustration at CSL’s sluggish share performance was evident at last October’s AGM, with investors almost kyboshing the remuneration report and delivering a 25 percent protest vote against the proposal to issue performance shares to Dr McKenzie.

A few issues to iron out

While management was clear about the future - or non-future - of the heart program, it was more equivocal about the headwinds faced by Vifor.

Dr McKenzie says the near-term growth aspirations for Vifor have been “dampened”, but maintains that in the longer term the business is just as promising as when it was acquired.

Space constraints preclude getting into detail, but the issues relate to reimbursement in the US, loss of exclusivity in Europe and the need for lower-margin products over more profitable ones. Some products in Vifor’s late-stage development pipeline did not meet clinical objectives.

Dr McKenzie says the business “continues to generate strong revenues and margins and synergies” while synergies [cost savings] are above expectations.

“While our strategic vision remains compelling [achieving it] will take longer than expected,” he chimes.

Vifor contributed $US1,006 million of half-year revenue - 13 percent of the group total - and a gross profit of $US670 million (15 percent of the total).

As with Resmed, CSL has also tackled concerns that the advent of ‘fat busting’ drugs such as Ozempic will crimp Vifor’s performance.

The rationale? There will be less diabetes and kidney disease.

Unlike with the sleep disorders house, the issue didn’t rate a mention during Tuesday’s results briefing. Last October, Dr McKenzie said he did not expect the obesity drugs to have a material impact on the business.

Arrested development

The $1 billion heart trial - the biggest in CSL’s history - enrolled 18,200 patients across 850 sites in 49 countries.

A plasma-derived infusion therapy, CSL112 was aimed at the 10 percent or so of heart attack victims who have a second attack within 90 days of the first.

The outcome of the trial was considered binary - the drug either would work or not - and sadly CSL112 proved no better than placebo in avoiding secondary heart attacks.

As the results were top-line only, we can’t know how big the miss, before they are aired at a US cardiac get-together on April 6. But there’s no suggestion the drug has a future with, say, a specific patient cohort.

Cracking hardy, CSL research and development head Dr Bill Mezzanotte says the learnings of the well-constructed trial would assist CSL’s other development pursuits.

“We are disappointed with the results, but not in the efforts of our people.”

During the half year, CSL spent $US669 million - 8.3 percent of its revenue - on research and development and has other potions bubbling away in the cauldron.

Dr McKenzie cites a pending phase III trial of clazakizumab, for end-stage kidney disease. By the end of calendar 2024, the company hopes to win approval for garadacimab (hereditary angio-oedema), while investors should also expect phase III data for the use of Hizentra for the rare disease dermatomyositis.

And lest we have forgotten about Covid – Cov-what?- the company expects to roll out enhanced vaccine across four geographies between 2024 and 2026.

CSL's Eu-Rika moment?

CSL's improved earnings were helped by a 10 percent reduction in the cost of collecting blood from donors.

During the pandemic, the company was forced to pay more for blood donations in the US, given folk were less inclined to leave home. Low unemployment also crimped the propensity of America's working poor to part with their claret.

CSL's weapon is Rika, a long-awaited plasmapheresis collection system that has been rolled out across 30 collection centres and is expected to be installed in all 300-plus US centres within 18 months. The project has been plagued by technical delays.

CSL is also seeking approval to extract 10 percent more blood from a donor. This would entail yaking blood based not just on the donor's weight, but other factors including the red cell count. In the words of one colourful analyst during an otherwise beige profit briefing: "You are sucking out 10 percent more volume from their veins as before."

Asked whether CSL would boost donor fees to reflect this, but Dr McKenzie notes that Rika has also reduced the donor's time in the chair by 30 percent. We will take that as a 'no' - but the party pies and sandwiches will stay.

According to broker Jarden, CSL's current collection system (Nexsys) costs an average $7 to $8 per donor in $A terms, but Rika could bring this down to as low as $1.

Dr Boreham's diagnosis:

This week's sell off looks a tad harsh, given management also reaffirmed expectations of a full-year profit of $US2.9 billion to $US3 billion (up 9-11%). But the company may have unveiled plans to start a business on the Moon, as investors weren't listening.

It's also worth remembering that while the heart news is a nasty jolt, most CSL analysts had not factored a successful heart drug result into their valuations in the first place.

As we posited after last year's interim numbers, CSL shares look perennially expensive but the company's performance has always justified the high trading multiples.

In the past, CSL used share buy backs liberally to improve earnings per share, but it no longer has buckets of unused cash. In fact, S&P Global Ratings grumbles about CSL's "heightened financial leverage".

CSL may have bled this week, but our Mr In Between view is that a steady flow of new products should staunch the wounds in the short to midterm. With a bit of iron will, Vifor's problems also look fixable.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. That's his perfect excuse for saying that his musings in no way constitute investment advice … and you can't suck blood from a stone.

NEUREN PHARMACEUTICALS

Neuren has rebutted claims by New York short-sellers Culper Research regarding the discontinuation rate of trofinetide licenced to Acadia and marketed as Daybue.

Last year, Neuren said that its North America partner Acadia Pharmaceuticals had US Food and Drug Administration approval for Daybue, or trofinetide, for Rett syndrome for adults and children two years of age and older (BD: Mar 13, 2023).

Today, Neuren said that Acadia was the subject of a research report by Culper Research "which disclosed that they hold a short position on Acadia".

The company said that there were "numerous analyst research reports published on Acadia and on Neuren, many incorporating surveys of US physicians, that present a different view to Culper".

Neuren said that in a presentation on January 9, 2024, "Acadia reiterated guidance for net sales of Daybue [for the three months to December 31, 2023] of $US80 million to $US87.5 million" ($A122.8 million to $A134.3 million).

The company said that net sales of $US67 million and $US23 million were reported for the three months to September 30, 2023 and June 30, 2023, respectively.

Neuren said that Acadia updated the data on persistence of Daybue treatment, with 76 percent remaining on therapy after six months based on confirmed discontinuations, or 68 percent based on confirmed discontinuations and patients who were 60 days past their scheduled refill.

The Culper Research report said that of 5,081 patients trying Daybue, 4,377 discontinued with 703 patients on the drug at the end of 2023, a rate of 13.8 percent.

Culper said "Acadia has misrepresented Daybue's safety profile, and in turn, patient retention rates".

The research report said that "Acadia's head of research and development, its chief science officer, and its general counsel have all left in the past three months".

Culper published a table of benefit with 37.8 percent of trofinetide patients showing improvement compared to 15.2 percent on placebo.

Culper highlighted in red that 62.3 percent of trofinetide patients had no benefit or were minimally worse, while the table showed that 84.9 percent of patients on placebo had no benefit or were minimally worse.

The report included a graph of projected Daybue revenue with the analyst consensus starting at $US369 million in 2024 and rising to $US827 million by 2030, compared to Culper's estimate of $US316 million in 2024 falling to $US227 million by 2030.

Neuren said that the after-hours Acadia share price on February 15, 2024 was up 1.19 percent.

According to Yahoo Finance, Acadia closed down 38 US cents or 1.49 percent at $US25.18 with 3.5 million shares traded.

Neuren said that Acadia's fourth quarter earnings announcement was scheduled for February 27, 2024, US Eastern Time.

Neuren fell $3.27 or 14.2 percent to $19.78 with 3.5 million shares traded.

RHINOMED

The ASX says Rhinomed has been removed from the official list, effective from the close of trading today.

Earlier this year, Rhinomed said that 98.79 percent of its extraordinary general meeting voted to delist from the ASX; and yesterday, the company said that it has requested a suspension ahead of delisting (BD: Dec 11, 2023; Jan 21, Feb 15, 2024).

Rhinomed last traded at four cents.

POLYNOVO

Polynovo says an undisclosed Government has ordered $US775,000 ($A1,189,000) of Novosorb BTM for full-thickness burns for use by Ukraine.
Biotech Daily believes the undisclosed government is neither Australia nor the US.
Polynovo said the Novosorb biodegradable temporizing matrix (BTM) order was its "largest ever single order", was ready for dispatch and would be used to treat wounded patients, with a second order expected, subject to distribution and product use.
Polynovo chair David Williams said "our recent support of countries in conflict zones has attracted interest from charities and foreign governments to financially assist in the provision of life saving devices like Novosorb BTM".
Polynovo chief executive officer Swami Raote said the company was "grateful to numerous surgeons, who have gone close to frontlines to treat the wounded and train Ukrainian surgeons in person, or virtually to use Novosorb successfully in makeshift operation theatre settings".
Polynovo was up 5.5 cents or 2.8 percent to $2.02 with 1.8 million shares traded.

CANN GROUP

Cann Group says the Auckland-based Rua Biosciences has begun legal proceedings against its subsidiary Cannoperations Pty Ltd.
In 2021, Cann Group said it would sell its interest in the Auckland-based Zalm Therapeutics to the Rua marijuana company for scrip (BD: Nov 30, 2021).
In 2022, the company said Rua had approved the proposed acquisition of Zalm Therapeutics, of which Cann owned 8.36 percent (BD: Jan 20, 2022).
Today, Cann Group said the proceedings related to a "dispute between Cann and Rua in respect of a manufacturing and supply agreement, which Cann has sought to resolve amicably with Rua, but which has escalated over time".
Cann said it "denies the claims brought against it and will vigorously defend the action".
Cann Group fell 0.4 cents or 5.3 percent to 7.1 cents.

QBIOTICS GROUP

Qbiotics says the US Food and Drug Administration awarded its intra-tumoral tigilanol tiglate drug for soft tissue sarcoma orphan drug designation (ODD).
Last year, Qbiotics said it treated the first of 10 patients in its phase II, open-label, single-arm, trial of intra-tumoral tigilanol tiglate for soft tissue sarcoma (BD: Jun 13, 2023).
Today, Qbiotics said orphan drug designation was for drugs considered potential treatments for patients with rare diseases, or less than 200,000 cases a year.
The company said the designation provided for a seven-year window of exclusive marketing rights following approval, exemption from user fees, eligibility for tax credits for qualified clinical trials and may potentially shorten clinical development due to closer collaboration with the FDA.
Qbiotics director Dr Victoria Gordon said "soft tissue sarcomas constitute a rare group of tumors comprising more than 80 subtypes that affect both adults and children".
"The prognosis of advanced soft tissue sarcoma patients remains unfavorable and new treatments are urgently needed," Dr Gordon said.
"The FDA orphan drug designation for tigilanol tiglate signals an important milestone for Qbiotics, reflecting its recognition by the FDA as a potential new treatment option for this debilitating and life-threatening disease," Dr Gordon said.
Qbiotics is a public unlisted company.

PHARMAUST

Pharmaust says the US Food and Drug Administration may approve monepantel for motor neuron disease with a single phase II/III trial.

Pharmaust said it had a pre-investigational new drug (IND) meeting with the FDA for monepantel for motor neuron disease, or amyotrophic lateral sclerosis, in preparation for a phase II/III trial in the months to June 30, 2024.

The company said the "FDA confirmed that Pharmaust may potentially receive accelerated and, or full approval from [the phase II/III trial] … subject to demonstrating substantial evidence of effectiveness and an adequate database supporting safety".

Pharmaust said the FDA advised it "that there were no minimum requirements for the number [of] patients and study sites located in the US".

The company said that the FDA advice meant that the study could include clinical sites and patients in Australia and Europe.

Pharmaust said the trial would be a randomized, placebo-controlled, adaptive clinical study evaluating the safety and efficacy of monepantel in patients with motor neuron disease, or amyotrophic lateral sclerosis, for 48 weeks.

The company said the primary aim of the study would be to assess the efficacy of monepantel, as compared to placebo, on the progression of disease.

Pharmaust did not state the number of patients it expected to enrol in the study.

Pharmaust chief executive officer Dr Michael Thurn said the company was "highly encouraged by the positive feedback from the FDA".

"It aligns with our expectations and provides the company with a clear understanding of the requirements to potentially receive accelerated and/or full approval of monepantel for treating [motor neuron disease, or amyotrophic lateral sclerosis]," Dr Thurn said.

"This advice truly positions us as a global play following the successful completion of our planned adaptive phase II/III clinical study," Dr Thurn said.

Pharmaust fell 0.5 cents or 2.2 percent to 22.5 cents with 3.15 million shares traded.

RHYTHM BIOSCIENCES
COMMONWEALTH SCIENTIFIC AND INDUSTRIAL RESEARCH ORGANISATION

Rhythm says the CSIRO has assigned the rights to a patent application relating to biomarker combinations used to detect advanced colorectal adenomas.

In 2018, Rhythm said it had begun a collaboration with the CSIRO for its Colostat colorectal blood test (Jan 24, 2018).

At that time, the company said it had its own reagents for most of the Colostat targets and the collaboration would develop the last key reagents required for the test, with CSIRO researchers to develop antibodies and target protein for the last of these targets and evaluate their performance relative to commercially available reagents (BD: Jan 24, 2018).

Today, Rhythm said CSIRO had assigned it any rights, title and interest in the patent the organisation held, which would simplify future steps for the company in both international patent applications and technology commercialization.

Rhythm chair Otto Buttula told Biotech Daily that the patent rights agreement was "largely a continuum of the previous licence agreement" with Rhythm taking the initial works forward and CSIRO assigning the rights to Rhythm.

Mr Buttula told Biotech Daily the deal fell "under the commercial terms of the last agreement".

Rhythm was up 1.5 cents or 12.5 percent to 13.5 cents.

MEDADVISOR

Compass I Topco, Kohlberg Kravis Roberts and Veritas Capital Fund Management says they have become substantial in Medadvisor with 43,999,999 shares (8.00%).
The New York-based Kohlberg Kravis Roberts said its related parties had acquired the shares as a result of its proposed indirect acquisition of Cotiviti Inc.
In August 2021, the South Jordan, Utah-based Cotiviti said it acquired 43,999,999 shares, or 11.66 percent of Medadvisor (BD: Aug 24, 2021).
Medadvisor was up 2.5 cents or 8.6 percent to 31.5 cents with 1.1 million shares traded.

IMMUTEP

Regal Funds says it has become a substantial shareholder in Immutep with 64,965,278 shares, or 5.46 percent.
The Sydney-based Regal Funds said it bought shares between October 24, 2023 and February 13, 2024, with the single largest purchase 6,174,562 shares for $2,268,534, or 36.7 cents a share.
Immutep fell half a cent or 1.45 percent to 34 cents.

GENETIC TECHNOLOGIES

Genetic Technologies says non-executive director Nick Burrows has resigned from today and that it is in the process of appointing two replacement directors.
Genetic Technologies said one of the incoming directors was based in the US and had “extensive consumer marketing experience in the women’s health area”.
Genetic Technologies chair Peter Rubinstein thanked Mr Burrows “for all his valued input into the company over four years and wish him well for the future”.
Genetic Technologies was down half a cent or 4.8 percent to 10 cents.