Biotech Daily

Friday August 16, 2019

Daily news on ASX-listed biotechnology companies

*** ASX, BIOTECH DOWN: LBT UP 8%; USCOM DOWN 9%**

*** DR BOREHAM'S CRUCIBLE: OPTHEA**

*** COCHLEAR REVENUE UP 7% TO $1,446m, PROFIT UP 13% TO $277m**

*** MEDLAB MARIJUANA EXTRACT NANABIDIAL 'SAFE, FAST-ACTING'**

*** JAPAN PATENT FOR NEUREN'S NNZ-2591 FOR BRAIN DISORDERS**

*** EXOPHARM SHARE PLAN RAISES $1.1m OF HOPED-FOR $2.8m**

*** RACE REQUESTS CAPITAL RAISING TRADING HALT**

*** ADMEDUS TELLS ASX 4C FUNDS QUERY: 'WORKING ON IT'**

*** REGAL FUNDS TAKES 12% OF OPTHEA**

*** CHO, UNLIMITED INNOVATION INCREASE, DILUTED TO 68% OF INVION**

MARKET REPORT

The Australian stock market slipped 0.04 percent on Friday August 16, with the ASX200 down 2.6 points to 6,405.5 points. Seven of the Biotech Daily Top 40 stocks were up, 24 fell and nine traded unchanged. All three Big Caps were up.

LBT was the best, up 0.7 cents or 7.5 percent to 10 cents, with 924,035 shares traded. Genetic Signatures and Oncosil climbed more than six percent; Avita improved five percent; Telix was up 4.2 percent; Cochlear and Orthocell were up more than three percent; with CSL, Ellex and Resmed up by less than one percent.

Yesterday's 4.8 best, Uscom, led the falls, down one cent or 9.1 percent to 10 cents, with 131,573 shares traded.

Next Science lost 8.8 percent; Compumedics and Kazia shed more than six percent; Actinogen and Pro Medicus were down more than five percent; Amplia, Cyclopharm, Dimerix and Patrys fell more than four percent; Alterity, Impedimed, Opthea and Starpharma lost more than three percent; Clinuvel and Universal Biosensors shed more than two percent; Medical Developments, Nanosonics, Neuren, Paradigm, Polynovo and Volpara were down more than one percent; with Cynata and Mesoblast down by less than one percent.

DR BOREHAM'S CRUCIBLE: OPTHEA

By TIM BOREHAM

ASX code: OPT

Market cap: $637.0 million

Share price: $2.55

Shares on issue: 249,789,839

Chief executive officer: Dr Megan Baldwin

Board: Geoff Kempler (chairman), Dr Megan Baldwin, Michael Sistenich

Financials (year to June 2019): revenue $914,840***** (down 20%), loss of $20.9 million (previously $16.9 million), cash of $21.5 million****** (down 33%)

***** Includes $750,167 of bank interest

****** Ahead of Federal Research and Development Tax Incentive of about $14 million

Identifiable major shareholders: BVF Partners 15.1%, Regal Funds Management 11.55%, Jagen Pty Ltd (Liberman family office) 7.3%, Baker Brothers Life Sciences 10.6%, Kifin Ltd 5.4%.

Coming after trial flops from Factor Therapeutics, Innate Immunotherapeutics and Bionomics, investors were awaiting the phase IIb results from the eye diseases house with more than a degree of trepidation.

They need not have fretted. Like Australian footy's OPSM (Optical Prescription Spectacle Makers) sponsored umpires, biotech's greater powers have a habit of evening up the score.

Released on August 7, Opthea's results for its OPT-302 combination treatment for wet age-related macular degeneration (wet ADM) were shown to be "statistically significant and clinically meaningful", opening up the prospect for a new drug for this hard-to-treat yet common affliction.

Opthea stock then closed 138 percent higher on the day at $2.06 a share, ascribing a $500 million valuation to the company.

But the buyers weren't done yet, with the shares closing the week at $2.79 for a chunky market cap of close to $700 million.

Reflecting the extraordinary interest, 160 listeners dialled-in to the company's conference call on the morning of the announcement.

“There were a lot of eyes on it,” says Opthea CEO Dr Megan Baldwin (pun unintended, presumably).

Given the global trial cost $40 million, a negative or ambiguous outcome would have met with a markedly different reaction.

Of course, there’s still much work to do. A phase III trial awaits and management is wasting no time approaching regulators to set the parameters for these studies.

So, what is wet age-related macular degeneration?

Wet AMD is marked by loss of vision caused by degeneration of the central portion of the retina (the macula). Blood vessels grow abnormally under the retina, resulting in leakage of fluid and protein from the vessel.

“It happens really quickly. Patients can see one week and then 10 days later lose their vision,” Dr Baldwin says.

A so-called trap inhibitor, OPT-302 is a fusion protein that blocks the activity of two proteins, vascular endothelial growth factors C and D (VEGF-C and VEGF-D). Opthea is developing OPT-302 as a combination therapy with the existing drugs Lucentis and Eylea, which block VEGF-A

“There’s a good understanding of the product, which validates our approach of targeting difficult pathways,” Dr Baldwin says.

About the trial

The trial, enrolling 366 previously untreated patients across 110 sites, aimed to test a combination of Opthea’s OPT-302 with the standard of care therapy, ranibizumab, marketed as Lucentis.

Relative to the control group treated only with ranibizumab, the randomized, double masked, sham-controlled trial showed a mean “visual acuity gain” after 24 months.

Randomized means the patients were split, like, randomly into four groups: those receiving OPT-302 and ranibizumab in a 0.5mg dose, ditto for 2.0mg, a sham injection in combo with ranibizumab and ranibizumab alone.

In lay folk terms, the lucky-duck OPT-302 with ranibizumab patients were able to read more letters on an eye chart: a mean 14.2 letters compared with 10.8 letters for the ranibizumab-only control group.

The result achieved a probability (“p”) score of 0.0107, bearing in mind that the closer to zero the less chance the results were a fluke, meaning that the result was 98.93% not just good luck.

Patients were treated with two intra-vitreal (injected) doses of 0.5mg and 2.0mg, with the low dose group having a similar result to the control group.

The primary endpoint was a “mean change” in visual acuity, as measured by the official standard known as the Early Treatment Diabetic Retinopathy Study (ETDRS) best corrected visual acuity (BCVA), also known as a standard eye chart

Opthea also claims victory with key secondary endpoints, including the proportion of participants gaining 15 or more letters on an eye chart.

Of those in the 2.0mg combo cohort, 45 percent gained 15 letters or more from the baseline, compared with 40.5 per cent in the Lucentis only group.

Also, 99.2 percent of the 2.0mg combo group achieved stable vision - defined as loss of fewer than 15 letters - compared with 96.7 per cent for the Lucentis only group.

‘A high bar’

Chief investigator and ophthalmic surgeon at King’s College London, Prof Tim Jackson, said the bar was set high in terms of the trial’s construction.

“OPT-32 may emerge as a combination treatment that can offer better vision gains than the standard of care,” Prof Jackson enthuses. “Further registrational trials are clearly justified.”

Dr Baldwin said the trial could have been constructed as a phase III registration trial !!!, but would have required dosing results for nine to 12 months and more safety data, which would have taken too much time.

The design of the trial, she said, posed sizeable hurdles.

“With two injections you have to be better [than the standard of care]. You can’t be equivalent and that’s why we went to the trial we did.”

Dr Baldwin said the trial was one of the biggest phase IIb studies ever carried out and was done under “tight” conditions with the masking of data. “We didn’t know the result until we got the email,” she said.

What’s next?

Not surprisingly, the company is planning its phase III trial, having already knocked on the door of European regulators to suss out what is required. The US FDA is next.

“We are doing all we can,” Dr Baldwin says. “You don’t want to waste any time on a trial program, because time is money.”

While the structure of the phase III study is undecided, it's likely to involve two trials of about 400 patients each, randomized to a control arm and a 2.0mg dosing arm.

The trial will "take all comers" rather than focus on patient sub-groups, thus expanding the indication of any commercialized product.

Meanwhile, Opthea is enrolling a targeted 108 patients for a phase IIa trial to test a combination of OPT-302 and aflibercept (marketed as Eylea) on untreated diabetic macular oedema (DME).

A smaller nine-patient, phase Ib effort met safety hurdles in July 2018.

The phase IIa study is being carried out at sites in the US, Israel, Latvia and Australia. The primary endpoint is a five-letter improvement after week 12, relative to the Eylea-only control group.

Affecting a younger, working age demographic, DME is a blindness-inducing condition that also involves retinal leakage. DME flows from diabetic retinopathy, which damages blood vessels in the retina to leak fluid.

The wet AMD market is about twice as big as the DME market, but both are commercially attractive indications.

Finances and performance

As of results Opthea had $20 million in cash and expects $14 million of Federal Research and Development Tax Incentive to roll in by the end of the year.

The company is fully funded for phase IIb trial close-out activities and the ongoing DME trial.

The company has enough money to "prepare for registrational phase III trial activities".

As for the phase III trial itself, the company won't see much change out of $150 million or so and all financing options - including partnerships - are on the table.

Opthea last went to the equity funding well in April 2017, raising $45 million after initial positive phase I wet AMD results.

Opthea also raised $13.3 million from in-the-money options in November 2014.

Unusually, recruitment for the wet AMD trial was completed six months early, which meant the results could be pulled forward from their scheduled 2020 release.

"The recruitment was phenomenal, which really helped our case," Dr Baldwin says. "We now have more [funding] runway than what we thought."

Fun fact

Opthea is the renamed iteration of Circadian Technologies, which is - or was - the first ASX-listed biotech, founded by biotech doyen Leon Serry and at one time including as a shareholder, Dr Alan Finkel, now Australia's chief scientist.

Circadian was "an incubator" for companies including the Victoria State-founded Amrad, later renamed Zenyth and sold to CSL. Other companies in its portfolio were Metabolic (which became Calzada before morphing into Polynovo), Antisense and Optiscan. With Mr Serry helping establish Dr Finkel's Axon Instruments.

Circadian dabbled in a number of applications including melatonin for jet-lag (hence the name), drugs for Alzheimer's and cancer diagnostics before deciding to focus on eye ailments. It acquired the VEGF portfolio a moment ago in biotech terms - in 2008.

Dr Boreham's diagnosis:

Opthea's diabetic macular oedema phase IIa results are expected in early 2020. Otherwise there may be a lull as the company does the dull but important stuff of parading the results at global ophthalmology conferences, such as EU Retina held in Paris on September 8 and an American Academy of Ophthalmology confab in October 12, 2019. There's also the arcane ritual of being published in learned peer journals.

The company notes that global sales of Lucentis and Eyelea last year were worth $US3.7 billion and $US6.2 billion respectively - and these can only treat about one-third of the wet ADM sufferers. The cancer drug Avastin, used as an off-label cheaper alternative, accounts for even more than that.

In essence, that is what's got the market hares running post last week's trial results.

While Opthea needs some big licks of dough to fund the phase III trial, at least it's in a position of strength.

"If you come from the basis of success you have many options, whether it's funding or partnering," says chairman Geoff Kempler.

Despite the price surge, major investors have been happy to buy at the elevated valuation.

When Dr Boreham last opined on Opthea back in April 2017, he said: "While it's nice to see Opthea with a sharp focus on the one drug, there's little for the company to fall back on if OPT-302 fails to shine."

He added the market would wait and "see" and, indeed now we all have seen the light on this one.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. But he likes to think of himself as a man of vision with his eyes firmly on the big picture.

COCHLEAR

Cochlear says revenue for the year to June 30, 2019 was up 7.0 percent to $1,446,100,000 with net profit after tax up 12.6 percent to $276,700,000.

In a media release, Cochlear chief executive officer Dig Howitt said the company "continues to target the delivery of consistent revenue and earnings growth over time" with strong growth in its services business.

"After four years of strong growth driven by a combination of market growth and share gains, our developed markets units were in line with last year, while emerging units declined," Mr Howitt said.

Mr Howitt said it lost market share in the US and Germany when a competitor product was launched, but regained sales on the launch of its Nucleus Profile Plus Series cochlear implant, which had been "well-received … [and] driven an uplift in sales".

"We expect strong growth in cochlear implant units in 2020, driven by a number of new products launched late in 2019 and the continued investment in market awareness and access activities," Mr Howitt said.

He said the company expected to report a nine to 13 percent increase in net profit after tax of $290 million to $300 million for the year to June 30, 2020.

The company said that revenue from the Americas and the Asia Pacific was up six percent each, with Europe, the Middle East and Africa up eight percent.

Cochlear said that its cochlear implant revenue was up two percent contributing 58 percent of total sales revenue, with services, including sound processor upgrades, composing 30 percent of sales revenue and acoustics, or bone conduction and acoustic implants responsible for 12 percent of sales revenue.

Cochlear said investment in research and development was up 10.0 percent to $184.4 million or 12.8 percent of total revenue for the year to June 30, 2019.

The company said the final fully-franked dividend was up 9.4 percent to $1.75 to be paid on October 14, for a record date of September 20, 2019, taking the full year dividend to $3.30 compared to the previous year's $3.00.

Cochlear said that basic earnings per share climbed 12.4 percent to $4.80 compared to the previous year's $4.27.

The company said net debt was up by 19.5 percent to $103 million and it had cash and cash equivalents of $78.6 million at June 30, 2019 compared to $61.5 million last year.

Cochlear climbed $7.91 or 3.9 percent to $209.43 with 401,630 shares traded.

MEDLAB CLINICAL

Medlab says a blinded, randomized, 16-patient, phase I, pharmaco-kinetic safety trial of its marijuana extract Nanabidial shows it is safe and fast-acting.

Medlab said that Nanabidial delivered with its Nanocelle platform had a 20-to-one ratio of cannabidiol (CBD) to tetrahydrocannabinol (THC) and was found to be safe, fast acting and positive for absorption and metabolism, achieving plasma concentrations quickly and with a half-life of four hours.

Medlab chief executive officer Sean Hall said his company was "one of a global few who possess proof via clinical studies that the Medlab patented pharmaceutical grade cannabis formulations are actually absorbed, what that absorption profile looks like, and how the product is utilized, metabolized and eliminated from the body over time".

"This is essential to regulatory efforts in proving the products efficacy, and more so to the medical community who require a detailed understanding of the body's utilization of any given pharmaceutical product," Dr Hall said.

Medlab fell 1.5 cents or 3.3 percent to 44 cents.

NEUREN PHARMACEUTICALS

Neuren says the Japan Patent Office has granted a patent covering its NNZ-2591 for the treatment of autism spectrum disorder and neuro-developmental disorders.
Neuren said the patent, titled 'Bicyclic compounds and methods for their use in treating autism spectrum disorders and neurodevelopmental disorders" would protect its intellectual property until July 2034.
Earlier this year, the company said that pre-clinical trials of NNZ-2591 in mouse models of Phelan-McDermid syndrome, Angelman syndrome and Pitt Hopkins syndrome showed potential efficacy (BD: Feb 18, May 17, 2019).
Neuren said there were no approved drug therapies for the three debilitating neuro-developmental disorders, which were caused by mutations or deletions in a different gene or chromosomal region.
The company said they shared common symptoms and an underlying impairment in the connections and signalling between brain cells.
Neuren fell two cents or 1.5 percent to $1.33.

EXOPHARM

Exopharm says it has raised $1,099,640 in a share purchase plan at 37 cents a share.
Last month, Exopharm said it had commitments for a $4,440,000 placement and hoped to raise a further $2,775,000 through a share purchase plan (BD: Jul 24, 2019).
The company said the funds would be used to accelerate its development activities for its exosome technology, across manufacturing, testing and additional intellectual property.
Exopharm was unchanged at 38 cents.

RACE ONCOLOGY

Race has requested a trading halt "pending an announcement regarding a capital raising".
Trading will resume on August 20, 2019 or on an earlier announcement.
Race last traded at 6.5 cents

ADMEDUS

Admedus has told an ASX Appendix 4C query that its "recapitalization plan has progressed but has not yet been finalized".
Admedus said it was "working with its advisors to complete the next phase of its recapitalization".
After the close of the market on July 31, the company filed its Appendix 4C quarterly report, which indicated that it did not have two quarters of cash (BD: Aug 1, 2019).
Admedus said receipts from customers for the six months to June 30, 2019 fell 29.7 percent to $10,106,000, with receipts for its Adapt products for the three months to June 30 down 45.6 percent to $4,133,000.
Admedus said it had a cash burn of $6,748,000 for the three months to June 30, with cash and equivalents of $4,887,000 and an estimated outflow for the three months to September 30 of $10,076,000.
The ASX asked Admedus if it expected to continue to have negative operating cash flows, what steps had been taken to raise further cash, if it believed it would be successful and if it expected to be able to continue its operations.
Admedus said it would provide further details when terms were completed.
Admedus was in an extended suspension and last traded at six cents.

OPTHEA

Regal Funds Management says it has increased its substantial shareholding in Opthea from 24,551,444 shares (9.84%) to 28,838,514 shares (11.55%).
The Sydney-based Regal Funds said that it bought the shares between June 20 and August 13, 2019, with the single largest purchase 3,063,120 shares for $7,964,112 or $2.60 a share.
Opthea fell eight cents or three percent to $2.55.

INVION

Unlimited Innovation Group says it has increased and been diluted in Invion from 2,968,894,000 shares (70.58%) to 3,739,652,180 shares (67.99%).
The Hong Kong-based Unlimited Innovation said that on March 19, 2018 it acquired 769,118,180 shares and was diluted in the eight-for-27, fully underwritten, non-renounceable $2,492,427 entitlement offer as part of a transaction with Cho Group for a stake in the company (BD: Apr 18, Sep 5, 2017, Mar 13, 2018).
The notice was signed by Cho Group principal Honsue Cho and Chiat Thian Chew and said the registered holders included Mr Cho, Mr Chew and Polar Ventures Limited.
Invion was unchanged at 1.5 cents.