Biotech Daily

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Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Amplia Therapeutics

By TIM BOREHAM

ASX code: ATX

Share price: 7.0 cents

Market cap: $19.0 million

Shares on issue: 271,609,233

Chief executive officer: Dr Chris Burns (co-founder)

Board: Dr Warwick Tong (chair), Dr Burns, Dr Robert Peach, Jane Bell

Financials (March quarter 2024): receipts nil, cash outflows $554,000, cash balance 3.385 million*, quarters of available funding 2.5

Identifiable major shareholders: Platinum Investment Management 14.54%, Blueflag Holdings 6.94%, Pengana Capital 5.6%, Acorn Capital 5.19%.

In its pursuit of a cancer drug for pancreatic cancer and possibly other indications including ovarian cancer, Amplia has history on its side given the involvement of its leading figures in a US-approved drug for blood cancer.

The therapy in question, Ojjaara (momelotinib) is a so-called janus kinase (JAK) inhibitor drug to treat myelofibrosis, developed by the formerly ASX-listed Cytopia.

The lead inventors were Melbourne based scientist and current Amplia CEO, Dr Chris Burns and Cytopia founder Prof Andrew Wilks.

In a typical case of ownership pass-the-parcel, Cytopia was sold to Canada's YM Biosciences for $14 million, the drug was acquired by Gilead for $US510 million ($A770 million) and then by Sierra Oncology (for a song).

Glaxosmithkline then acquired the drug through its 2022 purchase of Sierra for $US1.9 billion - the highest amount ever paid for an Australian-developed therapy.

The US Food and Drug Administration (FDA) green-lighted the treatment last year, thus creating history, with the drug arguably only the third locally-invented drug to be approved by the agency (the others were Biota's flu drug Relenza and Hatchtech's Xeglyze for head lice and eggs); the legendary Gardasil is a vaccine.

"It was a very interesting time," Dr Burns says.

Can history repeat itself?

Amplia certainly can't be accused of targeting the low-hanging fruit, in that pancreatic and ovarian cancers are notoriously hard to detect and to treat.

Amplia's lead compound, AMP945, targets fibrosis: the formation of excessive fibrous connective tissues that can impair the function of organs including the lungs, liver, heart and kidneys.

The company has orphan indication for both pancreatic cancer and idiopathic pulmonary fibrosis - another hard-to-treat condition.

Making Amplia Great Again

Amplia has an - er - interesting history.

In early 2018, the company was known as Innate Immunotherapeutics and it famously had just come a cropper with a phase II multiple sclerosis trial.

There's even a Trumpian tinge to Amplia's history, in that former Innate director and major shareholder Chris Collins was Donald Trump's congressional liaison.

If Donald is convicted on his current charges, he knows who to consult about life in the clink: Mr Collins was sentenced to 26 months' jail after pleading guilty to tipping-off his son that the MS trial was less than tickety-boo. (Eventually, he was pardoned by Trump during his presidency).

But not to worry. After considerable soul-searching the company acquired the privately owned Amplia and its FAK inhibitor program (more on FAKs later).

Amplia was owned by parties including the now legendary Dr Chris Behrenbruch, Dr Chris Burns and Peter MacCallum Cancer Centre researcher Dr Mark Devlin (now an Amplia scientific adviser).

Initially, the program was the work of the Melbourne based, Federal Government-funded Cancer Therapeutics Cooperative Research Centre. While developed here, the rights resided with Cancer Research UK. But the organization wasn't actively developing it, so Doctors Burns and Behrenbruch negotiated to re-claim the tech.

Dr Burns took over from Dr John Lambert as CEO in December 2022. Dr John had replaced Simon Wilkinson in June 2019.

Dr Burns has 30 years in drug discovery and development, including CEO positions at public and private companies.

Along the way, Dr Behrenbruch resigned from Amplia's board in 2020 to focus on Telix Pharmaceuticals - a sage decision given the radiotherapy outfit now has a $5 billion market value. He retains a significant shareholding.

Innate changed its name to Amplia shortly thereafter and bunkered down to focus on its current programs.

What the heck is FAK all about?

Amplia's lead compound AMP945 (narmafotinib) is a focal adhesion kinase (FAK) inhibitor.

Most cancer treatments are designed to attack tumors directly by either poisoning them, or starving them of nutrients. This is fine when it works, but tumors are cunning in that they tend to mount a defensive response which blunts the effect of many cancer drugs.

It is hoped AMP945 will suppress a bodily agent suspected of aiding and abetting the spread of tumors and fostering fibrosis.

AMP945 removes the protective shields, rendering the tumors more responsive to chemotherapy.

AMP945 was discovered at the former Cancer Therapeutics Cooperative Research Centre, with the help of scientists from Monash Institute of Pharmaceutical Services and Peter MacCallum Cancer Centre, St Vincent's Institute of Medical Research, the Walter and Eliza Hall Institute of Medical Research and the CSIRO.

A great team effort all round, guys and gals!

On trial (and we're not talking about Trump)

Dubbed Accent, Amplia's clinical trial efforts centre on a two-phase open-label combination trial for advanced metastatic or non-resectable (inoperable) pancreatic cancer.

A recently completed phase Ib dose-escalation study enrolling 14 patients dabbled with 100, 200 and 400 milligram deliveries and concluded that a 400mg dose was most suited for the phase IIa stage.

Combining AMP945 with standard-of-care generic gemcitabine and nab-paclitaxel (Abraxane), the phase Ib stage reported that six of the patients had a partial response, while the remaining eight patients had disease “stabilization” (they didn’t get worse).

Seven of the 14 patients continued their treatment for more than six months, with two continuing after 10 months. This compares with the historic median progression-free survival of five and a half months for the standard-of-care therapy.

The phase IIa safety and efficacy effort will take place at six local sites and five in South Korea (a popular geography for trials given the in-situ skills and a compact population of 50 million).

The study aims for 26 patients initially, before interim analysis in six to seven months.

In a May 15, 2024 update, Amplia said the trial was going to plan, with 19 patients enrolled.

“An interim analysis will be conducted to determine whether six or more patients on the trial record a partial response,” the company says.

If so, a further 24 patients will be enrolled taking the total to 50.

The most advanced patient to date has been treated for 300 days, with a best response of a 70 percent change from baseline.

The company expects to release interim data by September 30 this year.

Beyond that, the company has an open investigational new drug status with the FDA for a trial combining AMP945 with Folfirinox and is discussing potential funding with US pancreatic cancer charities.

Also known as Folfoxiri, Folfirinox is a combination treatment of four chemotherapy drugs (folinic acid, fluorouracil, irinotecan and oxaliplatin) and the preferred pancreatic cancer chemo in the US and most of Europe (but not in older patients because of toxicity issues).

Buying time

It should be stressed that with so many other cancer drugs, AMP945 is not pitched at a pancreatic cancer cure - it’s all about buying more quality time for the patient.

In February the FDA approved a Folfirinox variant called Nalirifox, a cocktail of four drugs for metastatic pancreatic cancer patients, who have not received previous treatment.

Trials of Nalirifox showed an overall survival of 11.1 months, a statistically significant improvement over the 9.2-month overall survival with gemcitabine/Abraxane.

“You don’t need to do much for the community to be enthusiastic about new developments,” Dr Burns says.

Based on its animal studies to date Amplia hopes it can do better - and with less toxicity than the standard of care, the generic gemcitabine and/or nab-paclitaxel (Abraxane)

“There’s very clear evidence from the literature that inhibiting FAK synergizes with the activity of gemcitabine,” he says. “We know if we put those together, we are supercharging gemcitabine activity.”

He says pushing out the overall survival out from seven months to 12 months or beyond would be a “profound improvement” on the standard of care.

“If we could add four months or more that would be fantastic - patients could make it to their next Christmas, or their daughter’s wedding.”

Ovarian cancer

Because pap/cervical smears do not pick up the condition, around 70 percent of ovarian cancers are picked up in late stage and mortalities are high.

“As with pancreatic cancer, ovarian cancer is highly fibrotic, it’s very difficult to treat and turns up quite late in testing,” Dr Burns says.

In October 2023, Amplia presented pre-clinical ovarian cancer data to the American Association for Cancer Research special ovarian cancer pow-wow held in Boston.

The mice model pertained to the highest grades of the disease, which account for 90 percent of all ovarian cancer patients.

The data “clearly demonstrated” that narmafotinib improved tumor growth inhibition in chemotherapy-resistant ovarian cancer, relative to the standard-of-care, called niraparib.

The company is eying an investigator-initiated study, by which Amplia supplies the drug while another party funds the study and finds the patients.

Dr Burns is encouraged that the Boston-based Verastem Oncology is about to get accelerated FDA approval for a combo FAK drug for ovarian cancer (defactinib).

However, Verastem is targeting a low-grade ovarian cancer (which affects about 10 percent of patients), while Amplia focuses on the remaining high-grade patients.

Thus, the Verastem program validates the FAK approach whilst not being a competitor.

Finances and performance

On May 15, 2024, Amplia said it had raised $4.27 million in a rights offer, with most of the proceeds to be used to fund the Accent trial. The two-for-five offer was struck at 5.5 cents per share. Investors put out their palms for $1.983 million, with most of the shortfall satisfied by underwriter Taylor Collison.

Director Dr Robert Peach also agreed to sub-underwrite up to $150,000 of shares and was allocated $105,000. Dr Burns and director Jane Bell cumulatively took up $78,000. The raising takes the company's cash kitty to around $5 million, which Dr Burns says is adequate to fund the trial.

The stock is well-supported institutionally with Platinum Investment Management, Pengana Capital and Acorn Capital all gracing the register.

Over the last 12 months, Amplia shares have declined from 11 cents in May last year to 5.7 cents in mid-May, this year. In the post-Innate era, the stock peaked at 80 cents, in March 2018.

Dr Boreham's diagnosis:

So far, the Federal Government's 'Made in Australia' push has centred on solar panels and critical minerals, but should it be extended to drugs as well?

"Despite years of government funding and academic work, not many drugs have got to phase III and only two have been approved," Dr Burns says. "Others developed by Australian companies were bought in or were natural products."

If Dr Burns and Amplia have their way, a third drug (for pancreatic cancer) will be proudly bearing the made – or technically, discovered – in Australia logo.

"The difference with this [compared with the myelofibrosis] drug is I want to drive it locally for as long as we possibly can and see more of the success come back to Australia."

Patriotism aside, the unmet need is startling. In the US, 66,000 pancreatic cancer cases were diagnosed last year, with 50,000 deaths.

The current cost of treatment in the US alone is $US6 billion and is estimated to grow to $US36 billion by 2036.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. This column was proudly made in Australia.