Biotech Daily

Friday January 31, 2025

Daily news on ASX-listed biotechnology companies

Dr Boreham's Crucible: Mesoblast

By TIM BOREHAM

ASX code: MSB

Nasdaq code (American depository shares): MESO

ASX shares on issue: 1,270,527,187; **Share price:** $3.17; **Market cap:** $4.03 billion

Chief executive: Prof Silviu Itescu

Board: Jane Bell (chair), William Burns, Prof Itescu, Dr Eric Rose (chief medical officer), Philip Facchina, Dr Philip Krause

Financials (December half 2024): receipts $US3.1 million (down 21%), cash outflows $US20.65 million ($US26.57 million previously), cash on hand circa $US200 million ($A322 million) after January's $US160 million placement

Identifiable major shareholders: G to the Fourth Investments LLC (Dr Gregory George) circa 18%, Prof Silviu Itescu 6.2%

Fresh from its landmark US regulatory approval for its stem-cell product for paediatric graft-versus-host disease (GvHD), Mesoblast plans to waste no time pursuing consent for the much bigger indications of heart disease and back pain.

Other inflammatory diseases such as irritable bowel syndrome (IBS) are also on the cards, along with adult GvHD.

For those who might have forgotten after a hazy summer, in December the US Food and Drug Administration (FDA) approved Mesoblast's Ryoncil for children two years and older who are resistant to the standard-of-care steroids.

The treatment is based on mesenchymal stromal cells (MSCs), a program Mesoblast acquired in 2013 (see below).

Ryoncil is the first GvHD stem cell therapy approved by the agency and the first of any sort of mesenchymal stem cell therapy.

Mesoblast founder and CEO Prof Silvio Itescu says the "historic" approval paves the way for Mesoblast to pursue the other indications.

"We have created a benchmark for the whole industry," he says.

Not wasting the moment, in January the company executed a $US160 million ($260 million) capital raising, by way of a placement.

Try and try again

Graft-versus-host disease affects about half of all allogeneic (off-the-shelf) bone marrow transplant recipients, affecting the skin, liver and gastrointestinal tract.

There are more than 30,000 bone marrow transplants annually, with about 1,500 childhood cases in the US. About half of them will develop GvHD.

In the case of patients resistant to the standard-of-care of steroids, mortality rates are as high as 90 percent.

GvHD is commonly treated with steroids, but this treatment is ineffective for many patients.

The approval marks third time lucky for Mesoblast.

In August last year, the FDA knocked back the so-called biologics marketing application and told the company to do another phase III trial. The same thing happened in 2020.

About Mesoblast

Mesoblast is using its proprietary mesenchymal lineage cell technology platform to develop allogeneic cellular medicines, to treat complex inflammatory diseases resistant to the standard of care.

These cells "respond to tissue damage, secreting mediators that promote tissue repair and modulate immune responses" the company says/

Mesoblast selects precursor and stem cells from the bone marrow of healthy adults, creating a master cell bank. This cell kitty is then expanded into thousands of doses for off-the-shelf use, without the need for tissue matching.

The cells can be administered to patients without the need for donor–recipient matching or suppressing the recipient's immune system.

The company's phase III product candidates are Remestemcel-L (Ryoncil), Revascor (advanced chronic heart failure) and MPC-06-ID (for chronic low back pain due to degenerative disc disease).

A slow-burn story

Mesoblast was founded by stem-cell expert Prof Itescu, based on technology developed over 10 years by the Institute of Medical and Veterinary Sciences (now South Australia Pathology) and the Hanson Institute in Adelaide.

Mesoblast listed on the ASX in December 2004, having raised $21 million at 50 cents apiece and then on the Nasdaq in late 2015.

In 2013, Mesoblast bought the intellectual property of US pharma group Osiris Therapeutics in 2013, for around $US100 million.

The company receives royalties or milestones on two non-US approved products: for GvHD in Japan (Temcell, marketed by JCR Pharmaceuticals) and for peri-anal fistulas in Europe (Alofisel, marketed by Tigenix). Perianal fistulas are a common complication of Crohn's disease.

In 2016, partner Teva walked away from a deal by which it would have funded the heart program (sending Mesoblast shares down 42 percent in a day).

Sod it! Let's approve it …

Ultimately, the FDA consent was achieved without any additional trials – but we're sure it wasn't a case of the agency saying 'Yes' simply so the company would go away.

In 2020, the FDA rejected the therapy despite an expert panel recommending the approval on a majority of nine votes to one.

"It's hard to say anything about that, other than those are the difficulties faced when you are first in class." Prof Itescu says. "For new products, the bar is higher than for traditional products."

Just released, a lengthy FDA document notes the 70 percent response rate was "significantly superior" to data generated from the approved non-stem-cell adult GvHD drug, ruxolitinib (Jakafi).

Prof Itescu says the FDA asked no fewer than 70 questions in the lead-up to approval and the company answered them promptly.

He adds the FDA has been clearer “in terms of their expectations and what we and others need to do (in terms of acceptable data.”

Roll up, roll up for the Ryoncil rollout

Given the “tremendous unmet medical need”, Mesoblast will waste little time making Ryoncil available in the US.

The quest is made easier because 45 percent of the top US transplant centres account for 77 percent of the potential market. Half of the transplants are done at 15 sites – an even more modest footprint.

Investors should expect an update “in the next few weeks” on revenue and reimbursement expectations.

Earlier, broker Bell Potter estimated peak sales of $US137 million annually.

Prof Itescu says that given Ryoncil’s benefit of almost 50 percent survival after four to five years, reimbursement should be like that of other recent US-approved stem-cell therapies.

The company has plenty of inventory at its Singapore factory, with targeted delivery to the centres within 48 hours “if not 24 hours”.

Heart approval next?

In 2020, a 537-patient heart trial missed the primary endpoint of reducing heart failure in chronic patients.

But a follow-up study identified strengthened heart function at 12 months among the “largest unmet needs and best responders”.

As reported recently in the European Journal of Heart Failure, a single injection into the left ventricle reduced the risk of heart attack, stroke and mortalities over a median 30 months and for as long as three years.

The company is hoping for FDA accelerated approval for patients with left ventricle assist devices (LVADs), which means it would be able to sell the product ahead of a confirmatory trial.

More than 100,000 US patients each year progress to end-stage heart failure, with a one-year mortality exceeding 50 percent.

Given the size of the market, the company expects to seek a commercialization partner.

Don’t forget the kids

Mesoblast is also targeting the children’s disorder hypoplastic left heart syndrome, for which it has rare paediatric disease designation.

“Spectacular” results of a randomized trial at the Boston Children’s Hospital showed an increase in the size and function of the children’s under-developed left ventricles.

“By doing that, we enabled a surgeon to create a permanent circulation by which the left ventricle supports he whole body,” Prof Itescu says.

The agency is likely to require another trial for the disease, which accounts for up to 40 percent of neonatal cardiac fatalities.

We’ve got your back

With lower back pain, the company is undertaking a phase III study to confirm the results of a 2021, 404-patient phase III trial, showing the therapy to be “safe, durable and effective”.

Specifically, the program is for chronic low back pain due to inflammatory degenerative disc disease, of less than five years’ duration.

The 2021 study showed a reduction in pain from a single injection with a duration of 12 months to three years.

“The FDA demanded a trial with the same endpoint – pain reduction at 12 months – so we have started second trial,” Prof Itescu says.

Key secondary measures include improvement in quality of life and function, with a focus on reducing opioid use.

The company has begun a 300-patient randomized, placebo-controlled study across 40 US sites. The placement funds enabled the sites to be expanded from the envisaged 15.

“That is a huge blockbuster, multi-billion-dollar opportunity in the US alone,” Prof Itescu says.

In Europe, the company is partnered with Germany’s Grunenthal and will seek a US buddy.

Finances and performance

Subscribed for by a mix of new and existing shareholders, the placement was struck at the going market rate of $2.50 per share.

The company now has cash on hand of around $US200 million ($322 million), enough for the next three years.

In the December 2024 half Mesoblast reported receipts of $US3.1 million, (down 21%) and cash outflows $US20.65 million, compared with a $US26.57 million deficit previously.

In the year to June 2024, the company lost $US88 million compared with a $US82.4 million deficit previously, on customer receipts of $US5.9 million (down 21 percent).

The company has raised equity on numerous occasions.

As of June 2024, the company also had just over $US113 million of debt, of which $US100 million was classed as long-term.

This is by way of debt facilities with Oaktree Capital Management and Nova Quest Capital Management, with varying terms and conditions (some of which have been adjusted along the way).

In December, the company was added to the Nasdaq biotechnology index.

Mesoblast shares have given investors more ups and downs than a Coney Island rollercoaster ride, having climbed from their record low of 25.5 cents in early February 2024, to $3.37 after December's approval.

The shares peaked at $9.57 on October 2011.

About 35 percent of Mesoblast's register is US based – and growing – while offshore investors account for about half of the shares.

Dr Boreham's diagnosis:

Mesoblast's long-suffering investors will be pinching themselves after the Ryoncil approval but – hey! – it's for real.

Prof Itescu dubs GvHD as the tip of the iceberg.

"I see it as a halo product for our mechanism of action, which is broad," he says.

"The FDA has acknowledged we understand the mechanism and we can use this product to expand into other diseases."

The placement takes the funds raised by Mesoblast since listing to well over $1 billion, but management won't reveal about the exact amount.

"The fact we have taken our products to phase III - and beyond - means we have retained the full value to date on all of our pipeline," Prof Itescu says.

"Whatever the type of [partnering] transaction, it will be on terms very favourable to us."

Prof Itescu says such truckloads of dosh are typical of those required to bring a drug to market – and the company also has two advanced ones to show for the money.

“No matter how much we have raised, investors can be very proud with what we have done with the capital.”

He adds that investors need to be better educated about the risks and funding requirements of a drug development program.

“Less than one percent of all publicly listed companies are ever going to get a product approved by the FDA,” he says. “Getting our approved was a huge hurdle to overcome.”

Now that Mesoblast has won back the faith of shareholders, it needs to walk the walk with its ambitious plans - something the company has not always achieved.

Disclosure: Dr Boreham is not a qualified medical practitioner and does not possess a doctorate of any sort. He tries to walk the walk, blisters permitting.