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CAPITAL PARTNERS

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Two investments for the next decade - and how we approach the life sciences

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Dear investors and well wishers,

The fund advanced 11.4% net in January 2020, which is a nice start to the year after our 24% return last year.

The software firms we were buying so heavily late last year rebounded strongly, Afterpay moved to new highs, and we had strong performances from ASX-listed life sciences companies like PolyNovo and Avita which are discussed in this letter.

Performance	year-to-date
Afterpay	39%
Alteryx	57%
MongoDB	34%
Twilio	30%
Shopify	35%
Polynovo	33%
Avita	59%

Boardrom Lunch Series

We're planning to host a limited number of investor boardroom lunches in Sydney and Melbourne over the coming weeks. If you would like to attend please get in touch with Anna Satouris at anna@fraziscapitalpartners.com .

Two Aussie innovators in the life sciences

In the wake horrific bushires in Australia, it's somewhat comforting to know that two local companies are revolutionizing the standard-of-care for serious burns - and that's just the beginning.

1. PolyNovo

When you have a serious burn over a large surface area and require a skin graft, to get the best healing outcome the surgeon needs to place a layer below the skin graft to ensure a decent scar outcome. This ensures the dermis (the underlying layer that provides elasticity, and houses nerves, fat deposits and blood vessels) heals well.

This is currently done with an animal collagen product, or not done at all. Integra in the United States makes the layer out of cow dermis, another firm in Europe uses pigs and apparently others have even used shark fins.

This is not ideal. These products are expensive, but more importantly, if the wound gets infected bacteria actually eat the animal layer, which for serious large surface area burns and injuries is quite a big deal.

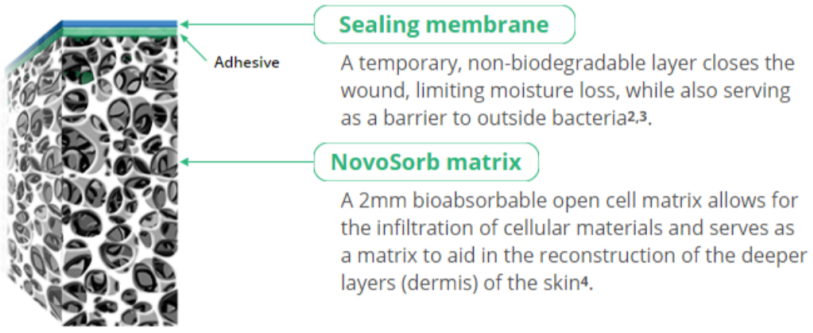
16% of burns treated using Integra (the incumbent competitor to PolyNovo) in their post approval study became infected, leading to several deaths. In a 149 patient study,

Integra's product failed to take in about 30% of cases, and animal products are simply too dangerous to use in cases like necrotising fasciitis (flesh-eating bacteria).

Enter PolyNovo.

The firm has a polyurethane polymer, Novosorb BTM (Biodegradable Sorbable Matrix) that can be used instead of the animal product. This is sterile, can be made into all kinds of shapes and forms, and is a fraction of the cost.

This turns a large wound into a series of micro wounds that heal quicker and better.



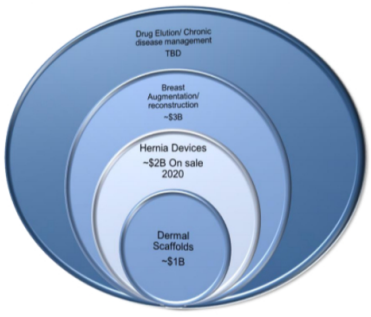
Within 1-2 weeks nerves and blood vessels begin to grow through the BTM, and remarkably, the polymer is completely absorbed and excreted by the body in about 12-18 months. Surgeons rave about the product.

Polynovo prices Novosorb BTM about 30% below Integra in Australia, and 50% cheaper in the United States. Our own channel checks suggest the pricing disparity is wider, (different medical centers can have different prices from the same providers). While conducting due diligence, a burns expert estimated that only about 40% of US hospitals use any layer at all, largely due to cost. By pricing their product well below competitors, PolyNovo hopes to expand the market size.

Integra makes about $600 million each year from their animal-sourced regenerative tissue products. PolyNovo's Novosorb BTM is cheaper, better, and given that it's a polymer, can be sold at gross margins of 90%.

PolyNovo was initially approved in the US for burns (about 50% of current use), but is already being used off-label for surgical reconstructions and trauma, such as in motorcycle accidents.

The best investments in the life sciences usually come from platform technologies, where an established technology can be applied to larger and larger markets. That is certainly the case here.



PolyNovo's polymers have clear applicability in hernias, which are common ruptures in internal organs. PolyNovo will file a 510k application with the FDA in the next few months (as Novosorb BTM is already approved, the approval process is simpler).

There are plenty of competitors, but again these are mostly animal products with poor outcomes, or non-dissolvable linings that come with their own set of issues.

NovoSorb's BTM could also be used in cosmetic surgery as a breast sling, to anchor the breast prosthesis during breast enhancements and reduce the likelihood of a harmful inflammatory response (which can be quite serious, and apparently happen

harmful inflammatory response (which can be quite serious, and apparently happen about 15% of the time). Again, the polymer's dissolvability is a strong advantage over alternatives.

PolyNovo has signed a deal with Establishment Labs to develop the technology. Establishment Labs will fund all sales, development and approval costs, and pay a royalty to PolyNovo. BTM could be used in chronic wounds, like diabetic ulcers, which again, is an area of enormous unmet need.

The next interesting application is in drug delivery. As the polymer dissolves at a consistent rate, and you can mix drugs to about 45% of the total, PolyNovo could create a long-lasting implantable drug delivery system. This would be useful in situations where daily medication is required, but compliance is an issue, like contraception, anti-psychotics, diabetes and treatments for blood pressure.

A possible strategy would be to partner with a generic drug producer to offer a unique and marketable delivery system for an off-patent drug at a very reasonable cost (the thing is a polymer, after all).

PolyNovo gives a pretty good idea of what we're looking for in the life sciences: proven technology, strong support from the medical community, significant value to the medical system, and clear scientific and economic fundamentals.

2. Avita

Avita is even more exciting.

Avita's products concern the skin graft layer on top of Integra or Novosorb BTM. The problem with skin grafts is that harvesting the skin creates quite traumatic wounds in their own right. You basically have to grate it off, and the wounds scar terribly. If the burn covers a large area, then the harvesting may need to be done more than once from the same spot… after waiting for the skin to grow back. I'll spare you the images, but Avita's investor materials paint a clear picture of the trauma and scarring involved in the current standard-of-care.

Pioneered by Dr Fiona Wood in Perth, Avita's RECELL device takes only one eightieth (1/80) of the surface area, and holds all the necessary materials to create a living layer of skin that can literally be sprayed on to the wound. The system includes all the necessary enzymes and buffers, and can be applied in about 30 minutes. Existing methods of growing sheets of skin from harvested cells can take weeks, and are barely used at all.

RECELL®
Autologous Cell Harvesting Device

This is all done in with the device above, and each can treat about 10% of a patient's body surface area. RECELL is already approved and sold in the United States.

As with PolyNovo, it's the next round of applications that are most exciting.

In burns treatment there's a trade-off between doing a skin graft and creating a second wound, or simply letting the wound heal on its own. A surgeon only grafts in more serious cases where the trade-off makes sense. Because RECELL creates a

substantially smaller harvesting wound, the device can dramatically expand the use of this kind of treatment.

An example is in paediatric scalds, where the negative consequences of creating a second scarring wound on a child ensures that surgeons avoid skin grafts save when absolutely necessary.

Avita can also modify the skin sample after it's been taken from the patient, which would enable the cure of terrible genetic disease disease like epidermolysis bullosa, where the skin blisters on minor friction. Avita could correct the genetic fault and spray on a living layer of the patient's own skin. These kinds of genetic treatments have been well established since we first wrote about them nearly five years ago.

The next set of opportunities are even more exciting, in another topic we've covered before: **vitiligo**.

There are two types of markets in pharma: **firstly**, where a certain number of people get a particular disease every year, and the total market size can be calculated accordingly. And **secondly**, where there is no existing treatment, so the market size includes everyone still living with the disease. These opportunities can be much larger.

There are over 7 million people in China with vitiligo and over 6 million in the United States. It's estimated that 1-2% of the global population gets the condition to some degree. Given there's no cure, statistics are poor, because there's little incentive to seek treatment. RECELL is already cleared for use in vitiligo in China, where two of Avita's studies were completed.

Avita's device can harvest skin from where there are pigment-producing melanocyte cells, and through a similar method as for burns, spray a living layer of skin over areas where melanocytes have died. There have been multiple trials and case studies around the world with excellent results for patients.

Vitiligo research has a couple of interesting features:

1. Patients can be used as their own controls, ie you can treat one part of a lesion, and not the other, and;
2. You can see whether the treatment worked by sight alone.

The opportunity in vitiligo is an order of magnitude larger than those mentioned previously. The cosmetic opportunity can be expanded further to the treatment of all hypopigmented scars, and even acne scars. Some clinics have already started offering RECELL commercially for vitiligo and other cosmetic treatments.

The next application of the technology is an order of magnitude larger again: skin rejuvenation.

As they say, the annual spend on anti-aging treatments is in the tens of billions - and none of it works!

Avita could harvest skin from say, the back of your ear, and spray on a new unwrinkled layer. All quite exciting - and plenty of ways for Avita to create value over the coming years.

Thorny Fund Management Question #3: How do you invest in the life sciences?

I've written extensively about our focus on technology companies with explosive growth and widely loved products.

These are certainly applicable in the life sciences, though there are other aspects we look for too:

1. Support from the medical community

There's a misconception that drugs and devices just need to be approved to start raking in dollars. But approval is only the beginning of the journey. Surgeons need to be convinced they should change their practice, and hospitals and end-payers need to be convinced the price is worth paying.

With a device like Avita's RECELL, the launch has to be done very carefully. If a sales

With a device like Avita's RECELL, the launch has to be done very carefully. If a sales rep convinces a surgeon to try the device, it's used incorrectly the first time, and six months later the outcome is sub-par, that surgeon is never going to use it again. This seems to have actually happened in the first markets Avita entered, but perhaps learning from that, the company is going much slower in the United States.

The trick here is to speak to doctors and surgeons to really get to the bottom of how they make decisions over whether to use this treatment or that.

2. Validation from Government and/or big pharma

The best forms of funding for biotech companies are non-dilutive grants from the Government. This is validation from perhaps the largest end buyer, and is basically free money.

Both PolyNovo and Avita are receiving funding from BARDA, the US Biomedical Advanced Research and Development Authority.

PolyNovo's pivotal trial for full-thickness burns is being funded to the tune of $14.6 million and counting, while Avita has received even more: A$68 million for pivotal trials in serious burns, paediatric burns and proof of economic efficiency.

3. Convincing in-human data

We only like to make serious investments in the life sciences when there is convincing in-human data. For both PolyNovo and Avita, clinicians are already using the product, so we have high confidence in the safety and effectiveness of the product.

Both PolyNovo and Avita's RECELL have been approved for conditions in the United States and around the world.

4. Staged, platform approach to value creation

The best opportunities in the life sciences involve a company developing a market leading technology, and then applying that tech to larger and larger markets.

Instead of going for larger markets first, Avita and PolyNovo have applied their product to serious burns, an area that has seen little innovation over the past decades and where competition is thin. In both cases surgeons have anecdotally begun using the tech off-label.

Approval in burns dramatically streamlines their entry into larger markets, where competition is fierce and stakes are higher. As shown in the Avita example, it is very hard to recover from a poor launch. These things need to be done right the first time.

Starting with burns looks a well-judged strategy.

5. Economic fundamentals

Both PolyNovo and Avita have very cheap raw input costs, and are used in complex plastic surgery. Shortly after their first approvals, margins are already high.

In controlled studies funded by the US Government Avita's RECELL treatment was proven to result in cost-savings of up to 30%, mostly by reducing the length of expensive hospital stays.

PolyNovo is yet to complete a controlled study on cost-effectiveness, but our industry channel checks suggest that cost savings are often much higher than the 30-50% stated by the company (each hospital or treatment clinic may receive different prices).

6. Intellectual Property

Our favourite situations are those where there is defensibility above and beyond patent protection.

Imagine the decision process of a generics provider assessing whether to build a copycat RECELL device.

It would need to be approved, but then the real work would start: convincing surgeons that it was not only equal to the existing standard of care, but superior, and worth the

change in practice. It would be competing against an incumbent that's innovating and developing the next generation of RECELL devices too. This is a very risky play, and very hard to justify the investment.

This is quite different to small molecule drugs, which are easily replicable, and once they're off patent, can be easily manufactured and sold. We have a very high bar for investing in small molecule drugs.

There are also some relevant quirks of the US medical system. In some situations surgeons are paid a proportion of the revenues from the services provided. Not particularly ideal from an efficiency point of view but occasionally relevant to companies selling devices like Avita!

This also came up in our work on Exact Sciences - their non-invasive diagnostic test competes with colonoscopies, which generate *substantially* more income for GI surgeons.

Outlook

Given that we've had a strong start to the year there's an inclination to trim and realise profits, but we're going to stick to our long-term investment philosophy. We are part way through the reporting season and so far our investment theses are on track.

I've been asked multiple times whether I'm selling some of our portfolio companies that have exploded in value, like Shopify. I'll send out a separate note with some updates on our reporting season and how we look at companies like this shortly. In short... no.

On the topic of podcasts, I recorded a fascinating chat with Matthew Shribman, an old chemistry pal from Oxford. We cover Twist Bioscience and some fairly novel science.

I also uploaded a podcast with Claude Walker of Ethical Equities, where we covered a number of fast-growing Australian companies, including the two featured in this letter, but also some we don't own, like Audinate and Pro Medicus (Claude was an early investor).

These are available on iTunes, Spotify, or your desktop.

A very warm thank you to all our investors and supporters.

Michael

If you'd like to invest with us in companies like PolyNovo and Avita (***before*** we send them out to the mailing list!), you can access our investment portal through the button below, or simply reply to this email and a member of the team will be in touch.

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