



Brisbane, 3<sup>rd</sup> October, 2016

Dear Shareholders,

I'm pleased to present you this quarterly update on our progress. It's been a busy period as we completed our manufacturing activities and prepare to launch our Phase II trial for VF-001 in the US. Our last quarterly update was predominately focused on the logistical aspects of moving our drug product manufacturing from Europe to the US. This has now been successfully concluded.

We are approximately a quarter behind schedule. Most of the delay has come as follow-on effect from the "out of specification" result obtained during material testing back in June (ASX Release 15<sup>th</sup> June 2016). Unfortunately, the resulting investigation, root-cause analysis and rescheduling of GMP testing "slots" pushed material release into the middle of the European summer, with a commensurate pace of completion by 3<sup>rd</sup> party vendors.

Notwithstanding the manufacturing delays and subsequent amendment of our IND, we have forged ahead with clinical trial preparation in parallel and we don't expect an adverse impact on either our ability to complete the clinical trial or the financial runway of the company per our financing plan. As indicated in our most recent set of annual financial statements, we have considerably reduced our cash burn rate and are employing effective cost control over product development.

Although the VF-001 Phase II trial in venous leg ulcers is the major focus both financially and operationally, we have made progress in many other areas that contribute to building the commercial profile of Factor Therapeutics. For example, we continue to evolve our intellectual property portfolio, both in terms of "ever-greening" strategies for our lead program, but also our general IP landscape around vitronectin-targeting growth factors. We have commenced a modest scope of work with our ocular program that should yield an initial set of results over the next 6 months.

As we head toward our Annual General Meeting in November, there is ample evidence that we are not the same company that we were a year ago.

Thank you for your support and engagement.

Sincerely

A handwritten signature in black ink, appearing to be "Nigel Johnson", written over a horizontal line.

Nigel Johnson, CEO

Level 19,  
179 Turbot Street  
Brisbane QLD Australia 4000

**phone** +61 7 3334 3900  
**fax** +61 7 3334 3999

**[www.factor-therapeutics.com](http://www.factor-therapeutics.com)**

GPO Box 1596  
Brisbane QLD Australia 4001



# Shareholder Update

## Introduction

The major focus areas for the company this past quarter was:

- ✓ Completing manufacturing and releasing the drug product for the upcoming Phase II clinical trial in the US. Fill-and-finish was completed in Massachusetts, USA by Berkshire Sterile Manufacturing (BSM) but we kept the release testing at Eurogentec S.A., part of Kaneka Corporation (Liege, Belgium) and SGS S.A. (Geneva, Switzerland) in order to avoid the cost of requalifying new testing vendors at this stage of development.
- ✓ Re-writing significant components of the IND in response to FDA feedback and requirements on CMC and comparability. This was conducted with the support of experienced Boston-based CMC consultants BPTC.
- ✓ Recruitment of a truly world-class medical advisory board and finalisation of the clinical protocol for the trial.
- ✓ Selection and start-up with our CRO : Parexel International (NASDAQ : PRXL).
- ✓ Lead investigator recruitment, site screening and selection, ethics submission preparation, etc., in readiness to formally commence patient recruitment as soon as the company is off clinical hold, pending FDA review of our amended IND.

## Phase II Trial : Progress Update

**We expect the IND amendments to be submitted to the FDA this week once the package has been reviewed and released by Parexel, our Authorized Representative.**

Parexel and Factor Therapeutics, in consultation with our Medical Advisory Board (MAB), have prepared a list of more than 100 potential investigational sites for the trial. Over 20 sites have declared an interest in being included in the study and approximately ~20 qualification visits will have been completed by the end of October. Previous VLU trial experience is a minimum requirement for participating Investigators.

We currently intend to include 26 sites in the study in order to maximize recruitment speed and quality. We have also selected a number of sites on the basis that the Investigators are important Key Opinion Leaders (KOLs) that we want to engage early and have them gain experience with the investigational product. Drug shipment and Site Initiation Visits (SIV) will commence shortly after the FDA lifts the Clinical Hold<sup>1</sup> and we expect that the first patient will be entered into the trial within 1 – 2 weeks after the hold is lifted.

Factor is working with Parexel to run our Investigator Meeting in early December in Miami (where there is a large concentration of wound care clinics) to further inform Investigators in the trial procedures as we roll-out beyond a few specifically selected sites. Implementation of the Silhouette® imaging system (<http://www.aranzmedical.com/>) to enable Investigators to accurately measure the wounds is well advanced in terms of integration with Parexel's data management system.

---

<sup>1</sup> Subject to FDA review and acceptance of the amended IND.

## Phase II Protocol : VF00102 in Venous Leg Ulcers (VLUs)

The final clinical protocol underwent significant refinement in response to input from our MAB. We have integrated three major objectives into the trial design:

1. Execution of a sufficiently sized, powered and structured study to be able to evaluate the efficacy of VF-001. The goal is to generate a data package that is sufficient to attract the interest of potential commercial partners.
2. Establishment of a sufficient efficacy signal to be able to strategize a Phase III trial design with the FDA for VF-001 as a biologic drug in the US. Part of the rationale of running an extensive multi-centre study in Phase II is to be able to move swiftly to Phase III if the commercial conditions warrant it.
3. In designing the Phase II protocol we have incorporated the SAWP<sup>2</sup> guidance from EMA, including sizing of the trial to demonstrate product safety and satisfactory end-points to demonstrate efficacy. With this study, assuming efficacy is adequately demonstrated, we would expect to be able to resubmit our CE Mark.



### **High Level Description of the Revised Protocol:**

- Randomised, double-blinded, placebo-controlled trial of VF-001 in moderately severe VLUs
- Three arms : placebo, "standard" dose (same as the previous clinical study) and high dose (10x)
- All arms receive both Standard Care (moisture dressings and compression bandaging) plus a weekly irrigation of either the placebo, standard or high dose. Placebo is visually identical to treatment, including appearance, colour, viscosity and packaging.
- 12 weeks of treatment with a 12-week follow-up period
- Primary end-point : % reduction in ulcer area
- Secondary end-point : proportion of patients with complete ulcer closure (EMA's preferred end-point) and an additional secondary end-point of pain reduction
- Enrolment target : ~170 patients randomised

In consultation with our MAB have decided to use the % reduction in wound area for the primary endpoint as it is an appropriate endpoint for non-pivotal US studies and affords the opportunity to strategize the design of Phase III studies by virtue of identifying the time-point at which the greatest difference occurs between placebo and VF-001. We will also be capturing pain scores and a basic QOLA<sup>3</sup> survey so that this efficacy study gives us the basis to start talking to European payers in conjunction with a CE Mark process in late 2017.

As soon as the FDA has approved our revised clinical protocol we will run a conference call to present the protocol and its objectives in more detail. A revised *clinicaltrials.gov* entry has been prepared and will be released in conjunction with the lifting of the FDA's clinical hold.

<sup>2</sup> Scientific Advice Working Party

<sup>3</sup> Quality of Life Assessment

For personal use only

## Ocular Program : Progress Update

At the time of completing the refinancing of the company, we conveyed to investors that we intended to expend a modest level of resource in building a future pipeline of advanced wound care products based on the company's core IP. We believe there are a number of high-value applications for both VF-001 and other molecules in Factor's stable of targeted growth factors.



There is a growing unmet need for ocular wound repair technologies – both in the surgical setting and in relation to certain disease conditions, some of which are potential orphan indications. We have initiated an initial R&D contract with Queensland University of Technology (QUT) to evaluate several candidates in basic models of ocular wound repair, including the use of relevant patient-derived cell lines. The project will involve a key researcher from the Queensland Eye Institute (QEI), Professor Damien Harkin.

## Intellectual Property

The company continues to actively expand and invest in its intellectual property (IP) portfolio. This includes ever-greening strategies for the lead program as well as new protein constructs and application areas.

Since the last shareholder newsletter we have received a European notice of allowance (July '16) for "Fibronectin : Growth Factor Chimeras" with broad claims around protein structures, host cells comprising genetic construct, compositions, and various applications. This follows patent grants in AUS, NZ and US.



The company also received European Certificate of Grant 2357195 (Aug '16) for "Growth Factor complexes and modulation of cell migration and growth" This relates to the VN-IGF commercial embodiment (VF-001) and is a divisional of the already granted parent IP reinforcing the background science of our lead program. Claims include complexes of vitronectin, IGF-1 and IGFBP3 – any composition, implant, wound or burn use, in vitro, skin replacement, agonist or antagonist of the complex comprising growth factor and fibronectin or vitronectin.

## R&D Tax

As part of the corporate turn-around of the company, we engaged Deloitte to review the company's historical R&D tax filings for 2012-15 as there were concerns about how management had classified research activities. As a result, the company has prepared lodgements for an expected net benefit to the company of ~\$820,000 from revised claims. The company has also obtained an overseas finding for the US clinical trial. For 2016, the company anticipates a refundable R&D tax offset of ~\$1M on the basis of R&D deductions of ~\$2.5M (subject to ATO review).



For personal use only

## Human Capital

With a rapidly growing third party vendor and contractor base as we head toward clinical trial launch, a higher level of finance function support is required to control project costs and effectively manage runway as we go into a period of higher burn rate. As such we decided that it was time to relieve Saskia Jo of the company secretary activities so she can focus more on supporting the project management team. To this end we announced the appointment of Melanie Farris (ASX Release 29th September 2016) as company secretary. Melanie has a significant amount of corporate governance experience in the life sciences space and is a welcome new member of the team.

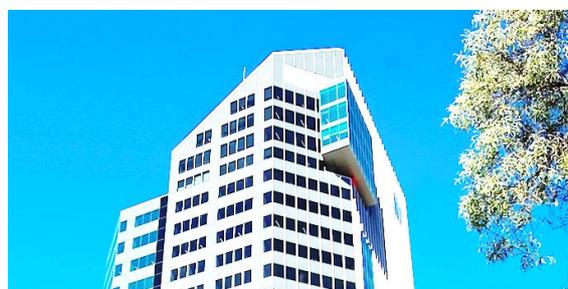


On the 14<sup>th</sup> of September we announced the appointment of Dr. Robert Ryan as a Non-Executive Director. Rob is a superb addition to the team and was recruited both for his regulatory and domain-specific knowledge of wound care and dermatology, and his transaction experience in our space. Both the commercial and drug development attributes were identified as “areas for improvement” in our recent board skillset assessment. With the company back on track with clinical development and the board able to return to a more strategic and forward-planning mode of action, we are certainly taking a fresh look at board structure and composition.



## Premises

Amidst a soft commercial property market in Brisbane, we have executed a term-sheet to sublease the Turbot Street office to a high-quality tenant. The company has occupied premises that were not appropriate for an ASX-listed company with a \$40m market cap and as part of reducing the cost-base of the business we had decided that the company needed a more modest office space.

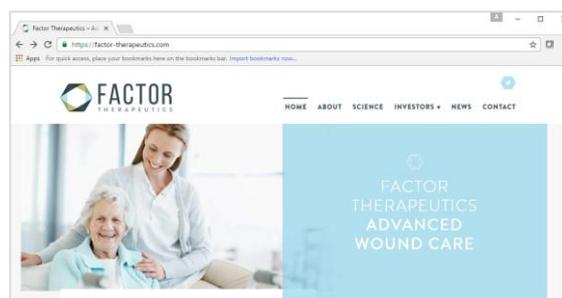


The company is considering two alternative office locations that are convenient for staff and business partners. The net benefit obtained from the subleases will finance ~2 years of occupancy at new premises, contributing to our runway and helping to reduce long-term liabilities.

## Corporate Website

Our new website is up at:  
[www.factor-therapeutics.com](http://www.factor-therapeutics.com)

Although we are still tweaking content and structure, we think it is a big improvement and showcases the company’s new image. A Spanish language version will also be up soon in order to provide patient information for our up-coming US clinical trial.



For personal use only

## Shareholder FAQs

*As we start to receive increasing interest in the company from new and existing shareholders, we have received a number of queries that we think are generally worth answering in more detail. To the extent that shareholders reach out with good questions (that are not commercially sensitive) we will add to this FAQ in future newsletters.*



In the financial report for year-ended 30<sup>th</sup> of June, the company reported an operating loss of \$11,612,031, which included a one-time non-cash impairment of \$7,485,691 for inventory disposal. Why did the company have to dispose of this material? Couldn't it have been used somehow?

VF-001 is a recombinant protein and it has a limited shelf life. Although the product is very stable we currently measure (validate) the shelf life as being 24 months. When the company filed its CE Mark application back in 2014 it had to demonstrate to the European Medicines Agency (EMA) that it had a validated process for manufacturing and, as such, had to spend the money on "at scale" production runs as part of its regulatory submission. Because the company assumed it was going to be shortly commencing commercial sales, sufficient inventory was produced to initiate sales. This inventory was actually very modest.

The accounting cost of the inventory is not the market value of the product, but the cost to develop the production process and manufacture the material. The inventory that we disposed of was manufactured to the standard required by EMA, but not the standard required by the FDA. Although it is the same "bulk" product, the FDA has very different requirements for how a product is characterised and ultimately packaged for use. As such, we were not able to use any of that inventory for clinical trials run under a US IND (even if we added sites in Europe).

There was no way that the inventory was going to be useful in any commercial time horizon, even with a successful resubmission of a CE Mark. It was costing the company several hundred thousand dollars a year to store, manage and test (stability test) those materials and so writing off the inventory was an unfortunate – but straightforward – financial decision. The material was destroyed because it is not approved for clinical use and we would not want the material to be used in any way that the company did not have absolute control over.



The company's burn rate seems to have been considerably reduced, even though the company is gearing up for a major clinical trial. How is this possible?

The company's previous burn rate was based on the premise that it was getting ready to initiate commercial release of a product. The company spent considerable financial resources preparing for a commercial launch with efforts on market-readiness, economics, reimbursement strategy, etc. The company had a larger staff base and because it was in commercial readiness mode, was expending considerably more financial resources on manufacturing and business development.

Over the past 12 months we have cut back expenditure in almost every operational aspect of the business. We have prudent cost control over travel and discretionary expenditure. We have cut back on staffing and compensation has generally been more modest. We have been judicious about the use of contractors rather than building an in-house team, wherever possible. We have scaled back manufacturing to a "phase appropriate" level, which is fundamentally lower cost than the production scale two years ago.

For personal use only



The company has been developing “VitroGro” for over a decade, surely by the time they are ready for market, there isn’t much IP protection left?

There are three parts to answering this question. The first is that the company continues to expand its intellectual property base, both in existing (i.e. lead product) and new areas. We have a very modest ongoing R&D expenditure that is predominantly for the purpose of ever-greening our IP by obtaining specific, targeted pieces of scientific data to support additional filings. Our lead program currently has commercially meaningful patent life in major markets and some of our newer filings confer IP protection out past 2030.

Secondly, our products are biologics. This means they are manufactured using proprietary cell lines. Unlike small molecule drugs and peptides, our products are very difficult to duplicate because the manufacturing conditions are complex. We have a lot of knowledge around how to control the production of our product that doesn’t appear in scientific publications or patent disclosures and this makes the production of generics more challenging.

Thirdly, VF-001 is classified as a biologic drug in the US – our major market. Generic copies or “biosimilars” cannot be filed until 4 years after the biologics licence application approval (BLA), and cannot be approved until 12 years after BLA. This 12-year period takes account of the increased regulatory approval requirements due to the more complex nature of the drug and is an important additional item of protection for our products.



Is VF-001 (VitroGro) a drug or a device? It’s confusing.

The answer is “it depends”.

In Europe, our product is classified as a Class III, Rule 13 device. This is a device that incorporates an “ancillary medical product” (Rule 13). In the case of VF-001, this ancillary medical product is the IGF-1 portion of the molecule. The European regulator as accepted that the vitronectin component of VF-001 is a “matrix protein” that anchors the IGF-1 (the medical product) to the wound bed.

In the US, the FDA’s Center for Biologics Evaluation and Research (CBER) has classified VF-001 as a topical biologic drug and, as such, Factor must develop VF-001 under an Investigational New Drug (IND) application. The difference in designation reflects policy differences between regulatory organisations. We could elect to change our designation in Europe to be consistent with the US, but there is really no short-medium term benefit in doing so.

The main theoretical advantage of being classified as a drug, other than market exclusivity periods (see previous question), is that it may enable the company to attract a higher price point in order to recover the cost of product development. However, our initial target market of Venous Leg Ulcers (VLUs) is a very large market opportunity that can very profitably support either drug or device price-points, especially because the cost of manufacturing our product is very low.



Why doesn’t the company refer to the lead product as VitroGro anymore?

The company had previously felt that using a “brand” enabled it to build visibility and awareness of the product with potential customers, especially as it approached commercial stage activity. This philosophy doesn’t apply in the context of the FDA because at

For personal use only

each phase of product development, there can be subtle tweaks to the product that actually means each “generation” of development is a distinct product from a regulatory vantage. As a general concept, the FDA doesn’t like seeing “brands” in regulatory documentation and, in fact, there is a real process involved in naming drugs – particularly biologics.

Factor’s current position is that “VitroGro” does not adequately explain or differentiate the lead product. VitroGro is fairly weak in terms of brand strength and trademark landscape. Naming drugs is not something typically done until later in the development process. Also, because the final product sold in the US may have a very different regulatory status than the product sold in Europe, we need a much more sophisticated branding strategy to cover both markets, hence the adoption of “VF-001” for the time being.



**The company has had roughly a three-month delay in getting the IND filed for the Phase II study. What has caused the delays?**

Most of the delay has come from the “Out of Specification” (OOS) result obtained as the result of packaging contamination of test samples (ASX Release 15th June 2016). The resulting investigation and root cause analysis (and documentation) took us almost a month to complete and required rescheduling lab testing to a later date.

Several of the release assays for VF-001 are quite complex tests that require significant lab time on sophisticated equipment that cannot be arbitrarily rescheduled. Although our vendors worked very hard to respond to our needs, the effective result was that testing was pushed into the middle of the European summer vacation, with commensurate delays.



**The company has repeatedly talked about a benchmark price of USD \$1,000 for their product. This seems very inexpensive for a novel drug?**

This is a common point of misunderstanding. When the company conducted pharmacoeconomic studies (some of which will be shortly published), “comparable” products were used to set a price point to test economic viability. To build a conservative business case, the company benchmarked a bundle of topical products currently used in chronic wound care. This benchmark price of €1,000 was tested in reimbursement models against assumed product efficacy. This doesn’t mean we would sell the product for €1,000 (or \$1,000 or £1,000) but rather that the current efficacy of the product supports this price point by eliminating weeks of compression bandaging and moisture dressings (standard care).



**The company hasn’t talked much about CE Mark recently. What’s the game plan?**

A CE Mark resubmission is absolutely a future objective. We have designed the Phase II trial of VF-001 with the CE Mark submission in mind, even though the data is collected in the US under an IND. We have done everything we can to make sure that this data set will be able to be incorporated into future European regulatory submissions. It’s a major opportunity for the company and we believe that the historical expense of manufacturing scale-up can still be captured.

For personal use only



## Upcoming 2016 Dates

- End-October : Update on FDA allowance of IND (~1 month delay from previous shareholder newsletter)
- First week of November : Clinical trial information conference call (planned), guidance on first-patient-in (FPI)
- 23 November : Annual General Meeting (Brisbane)
- 8-11 December : Factor Therapeutics is a sponsor and presenter at the Innovations in Wound Healing conference, Florida (USA)



---

### Corporate Contact

Dr. Christian P. Behrenbruch  
Executive Director  
Factor Therapeutics Limited  
@: [c.behrenbruch@factor-therapeutics.com](mailto:c.behrenbruch@factor-therapeutics.com)

### Investor Relations Contact

Kyahn Williamson  
Head of Investor Communication  
WE Buchan  
@: [kwilliamson@buchanwe.com.au](mailto:kwilliamson@buchanwe.com.au)

### About Factor Therapeutics

Factor Therapeutics Limited ("Factor") is a biomedical technology company that is developing treatments for acute and chronic wound healing applications. Factor is a clinical stage company with its lead program (VF-001) in Phase II for the treatment of venous leg ulcers (VLUs). The company's platform technology originates from the Institute of Health and Biomedical Innovation at the Queensland University of Technology, Australia. Factor's shares are traded on the Australian Securities Exchange (ASX) under the ticker FTT. For more information, please visit [www.factor-therapeutics.com](http://www.factor-therapeutics.com).

### Important Information

This announcement does not constitute an offer to sell, or a solicitation of an offer to buy, securities in the United States, or in any other jurisdiction in which such an offer would be illegal. The securities referred to herein have not been and will not be registered under the United States Securities Act of 1933 (the "US Securities Act"), or under the securities laws of any state or other jurisdiction of the United States and may not be offered or sold within the United States, unless the securities have been registered under the US Securities Act or an exemption from the registration requirements of the US Securities Act is available. This document may not be distributed or released in the United States.