Q&A with Ian Crosbie, CEO

Sequana Medical reported positive interim results from the POSEIDON study in 2020. Why are these so encouraging?

The interim POSEIDON data are really important because they give the first potential insight into the study outcome and specifically the endpoints that the FDA and Health Canada will use to decide on approval of the **alfa**pump. In these first 13 patients from the POSEIDON Roll-In Cohort, we reduced the need for therapeutic paracentesis by more than 90% compared to baseline and indicated a clinically relevant improvement in quality of life. The FDA and Health Canada have set a 50% reduction in therapeutic paracentesis as one of the primary efficacy endpoints for the study so you can see why more than 90% is so exciting for us. We hope to continue the positive results seen in these first POSEIDON patients and deliver a positive outcome to this study so that we can bring the benefits of the **alfa**pump to patients in the U.S. and Canada as soon as possible.

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Why is therapeutic paracentesis such a problem to treat?

Therapeutic paracentesis is the mainstay in chronic clinical management of refractory liver ascites - it has been used since the time of the ancient Egyptians and has not changed much! It is a painful and invasive procedure in which a large-bore needle is inserted into the abdomen to drain the fluid. It has to be done in hospital under medical supervision and can take five to seven hours. Unfortunately this does not stop the accumulation of the fluid and the drainage needs to be repeated every couple of weeks, so it has a severe impact on patients’ quality of life and creates a huge burden on already stretched healthcare systems. An equally important problem is the huge impact of the ascites accumulation on these patients in the days leading up to the drainage. Imagine trying to eat, sleep, breath, move, use the bathroom or in fact do anything when you have 10 – 15 litres of fluid in your belly! We estimate that half of the patient’s remaining life is “lost” due to the burden of this terrible condition and we believe that we can give these patients their life back and enable them to do the things that they want to do – maybe visit friends or family, travel, work in the garden or dance. With our **alfa**pump, we provide a 21st century solution for this debilitating condition and help these patients live a higher quality life.

Sequana Medical is developing a second product, alfapump **DSR. What does it address and how does it work?**

The **alfa**pump DSR is built upon the proven **alfa**pump platform, to deliver a fully implanted system for our proprietary Direct Sodium Removal (DSR) therapy. The intention is that heart failure patients suffering from fluid overload will have the system implanted for years and will be able to manage their fluid overload without the need for hospital visits.

DSR is a simple and elegant therapy that works in partnership with the body to reduce fluid overload. We extract sodium from the body using the DSR infusate and then the brain and kidneys work to quickly and accurately remove exactly the right amount of water from the body to maintain the correct concentration of sodium in the bloodstream. The fluid that the body removes is how we reduce the fluid overload.

You also reported impressive interim data from the RED DESERT study in 2020. Why is this trial important and what is so encouraging about the results?

First of all, it’s worth noting RED DESERT is a bold trial design, as we have set out to demonstrate for the first time that repeated dosing of DSR therapy using our **alfa**pump DSR system is both safe and effective. In five heart failure patients who were all on high doses of loop diuretic drugs, we stopped these drugs and were able to maintain their sodium and fluid balance just using DSR therapy. These results support our fundamental DSR hypothesis: our DSR therapy removes sodium from the body and then the kidneys step in and eliminate free water to maintain the correct sodium concentration in the blood. Moreover, by replacing their high dose loop diuretics with repeated dose **alfa**pump DSR therapy, we could restore the patients’ response to much lower doses of diuretic therapy – and this effect lasted many months after the DSR therapy ended.

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Can you tell me more about this restoration of the diuretic response in the patients treated so far in the RED DESERT study?

Over time, the kidneys of these patients stop responding effectively to diuretics, requiring higher and higher doses – which exacerbates the problem. These data have shown that by giving the kidneys a diuretic “holiday”, their response to diuretics can be restored. Diuretic resistance, in other words a poor response to diuretic drugs, is a common problem of heart failure patients and leads to fluid overload, also known as congestion, which is the most common cause of hospitalisation for these patients. These first five RED DESERT patients had an objectively poor response to diuretics at the start of the study but after six weeks of treatment with **alfa**pump DSR their diuretic response was restored to near normal levels. This is a really exciting aspect that we will be exploring further both in heart failure and other disease areas.

Beyond heart failure, what other indications are you looking at?

We are looking at new indications such as kidney disease / renal failure. For example, in hemodialysis the hemodialysis machine is doing two things – first it is removing the uremic toxins from the blood, but also it is seeking to control the fluid and sodium balance in the body. While hemodialysis is very good for removing toxins, in some patients it is less effective in maintaining the fluid and sodium balance or it may require very long sessions to remove sufficient fluid or sodium. We are supporting a study that evaluates **alfa**pump DSR in hemodialysis patients as a first step toward expanding the use of **alfa**pump DSR in hemodialysis.

In the longer term, we believe there could be the possibility to reduce kidney failure caused by high doses of loop diuretics – often when they are trying to maintain a damaged heart. If we could reduce the use of loop diuretics through regular DSR therapy, we may be able to delay or even avoid the need for hemodialysis and all the associated cost and quality of life impact on patients that it involves.

How important was the year 2020 for Sequana Medical? What feedback did you receive from investors?

We have taken very important steps in our journey to revolutionise the management of fluid overload when diuretic drugs are no longer effective and raised our profile with both local and international high-quality investors. There is a growing understanding and excitement for the commercial opportunity in both liver disease and heart failure as we explain the size of the potential markets, the clear clinical need and the limitation of the other treatment options. Investors have been impressed by our track record of delivering on our commitments and by the growing body of clinical data.

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