PRESS RELEASE
REGULATED INFORMATION – INSIDE INFORMATION

Sequana Medical announces presentation of positive DSR clinical proof-of-concept data demonstrating potential in volume overload due to heart failure

- **First-in-human single dose DSR study meets primary and secondary endpoints**
  - **Direct Sodium Removal (DSR) was safe & well-tolerated**
  - **Substantially higher sodium removal with DSR vs standard Peritoneal Dialysis (PD) solution**
  - **Consistent results between treated patients**
- **First clinical study of repeated dose DSR with alfa**pump® **(alfa**pump **DSR) planned to commence in H2 2019**

Sequana Medical management and Dr. Jeffrey Testani to host a conference call and webcast today at 14:00 CEST / 08:00 ET

Ghent, BELGIUM – 27 May 2019 (08:30 CEST) – Sequana Medical NV (Euronext Brussels: SEQUA), a commercial stage medical device company focused on the development of innovative treatment solutions for the management of liver disease, heart failure, malignant ascites and other fluid imbalance disorders, today announces the presentation of the positive results from the first-in-human single dose DSR proof-of-concept study for volume overload due to heart failure. The investigator-initiated study was conducted by Dr. Jeffrey Testani of Yale University. The study demonstrated that single dose DSR therapy in humans was safe and well-tolerated and resulted in a clinically relevant removal of sodium with consistent results between treated patients.

A key problem in treating patients with volume overload is that the removal of fluid without the removal of the associated sodium only results in a temporary benefit. Sequana Medical's innovative DSR therapy removes the sodium and then the body eliminates the associated fluid to restore the sodium concentration, resulting in sustained fluid removal. Data from this study demonstrate that DSR can result in the removal of large quantities of sodium and fluid in a safe and tolerable manner. This underscores the potential of Sequana Medical's **alfa**pump DSR to deliver a new and convenient treatment option for patients with volume overload due to heart failure.

The results have been presented during the late-breaking abstract session at the Heart Failure 2019 congress in Athens, Greece, today at 08:30 CEST (09:30 local time in Athens), by Dr. Jeffrey Testani, Associate Professor and Director of Heart Failure Research at Yale University. The abstract and presentation are available on the Sequana Medical website.

Dr. Jeffrey Testani, Associate Professor at Yale University, commented: "There is a clear unmet need in the management of volume overload and congestion in heart failure patients. Loop diuretics are our current mainstay of therapy but the adverse effects of these drugs are well described and development of diuretic resistance leading to progressive volume retention is common. The results of this study, together with the previously reported animal data indicate that DSR is a promising candidate therapy in heart failure. We are optimistic that future research will demonstrate that combining the novel DSR treatment approach with Sequana Medical's established **alfa**pump platform will deliver a convenient and effective non-diuretic treatment option in heart failure."

Ian Crosbie, CEO of Sequana Medical, added: "With volume overload accounting for 90% of the one million hospitalisations for heart failure each year, it is clear that better treatment options are needed to address the

$13 billion in U.S. hospital costs for heart failure. These positive first-in-human results reinforce our beliefs in the potential of our proprietary DSR therapy. We are excited to drive forward the clinical development of **alfa**pump DSR, combining the accumulated positive results of DSR with our validated **alfa**pump platform. We can leverage our extensive technical and clinical experience from the cirrhotic ascites and malignant ascites markets to de-risk our **alfa**pump DSR development program in heart failure. We plan to commence the first clinical study of **alfa**pump DSR in the second half of 2019 as the next step in this breakthrough program."

First-in-human single dose DSR study design & results

The investigator-initiated study (clinicaltrials.gov NCT03801226) was conducted by Dr. Testani at Yale University, in 10 patients receiving peritoneal dialysis (PD) who underwent randomisation and crossover to DSR infusate (a sodium-free solution) or standard PD solution. One litre of either DSR infusate or standard PD solution was infused into the peritoneal cavity and left to dwell for two hours before being removed. The patient repeated the procedure with the alternate solution one week later.

DSR therapy was safe and well-tolerated during a single dose administration and met its primary endpoint of non-discontinuation of the protocol due to discomfort or adverse events, with similar tolerability to standard PD solution. Sodium removal with DSR was substantial, equating to approximately five grams (which is 2.5 days of dietary sodium) removed with a single two hour treatment, and significantly higher ($p<0.0001$) than what is achievable with standard PD solutions. Unlike what is typically seen with loop diuretics, the inter-patient variability was very low with DSR therapy. The fluid removal through ultrafiltration was also higher with DSR compared to standard PD solution ($p<0.0001$). As a result of the convincing positive and consistent results between patients, the study could be halted after ten subjects (initially planned for up to 20 subjects).

Individual safety parameters such as change in blood pressure, plasma potassium, bicarbonate, calcium and magnesium were similar between both solutions ($p>0.35$ for all). There was a borderline significant 1 mmol/L decrease in serum sodium from baseline to 120 minutes in the DSR group ($p=0.05$) but this resolved by 60 minutes after draining the solution ($p=0.34$). Plasma glucose increased with both DSR and standard PD solution ($p<0.3$ for both), but this was not different between solutions at 120 minutes ($p=0.08$). There was negligible removal of off-target non-sodium electrolytes such as potassium, magnesium, phosphorus and calcium with DSR.

Conference Call and Webcast

Sequana Medical management and Dr. Jeffrey Testani will host a conference call with a live webcast presentation today at 14:00 CEST / 08:00 ET. The webcast can be accessed here. To participate in the Q&A, please dial one of the numbers below, using confirmation code 676873. The webcast and conference call will be conducted in English and a replay will be available on the Company's website shortly thereafter.

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About Volume Overload in Heart Failure

Heart failure is a progressive disease that results in the heart being unable to pump enough blood and thereby supply oxygen to support other organs in the body. There are an estimated 6.5 million adults in the U.S. suffering from heart failure and this number is expected to grow to 8.0 million by 2030. Causes of heart failure include coronary artery disease, heart attacks, high blood pressure and faulty heart valves. Heart failure can disturb the normal functioning of the kidney diminishing its ability to excrete sodium from the body and triggering compensatory mechanisms that cause water retention resulting in volume overload. This causes patients with heart failure to commonly experience shortness of breath, fatigue, difficulty exercising and swelling of the legs, arms and face.

Volume overload in heart failure is a major clinical problem. There are approximately one million hospitalisations for heart failure annually in the U.S. and 90% are due to symptoms of volume overload. The treatment options are severely limited in those patients for whom diuretic therapy is no longer effective. This limitation is evident from the 24% hospital re-admission rate at 30 days from discharge. The estimated cost of heart failure-related hospitalisations in the U.S. alone is $13 billion per year.

Sequana Medical's proprietary DSR therapy is under development and is a novel approach to the management of volume overload in patients suffering from heart failure. DSR therapy involves the removal of sodium via diffusion from the body into the peritoneal cavity by administering a sodium-free solution (the DSR infusate) into the abdomen. As a result, the body responds to restore the sodium concentration in the body by eliminating the associated fluid via osmotic ultrafiltration (the movement of water, together with sodium, from the bloodstream to the peritoneal cavity) and/or urination, resulting in a sustained level of fluid loss.

The impact of administering a sodium-free solution to the peritoneal cavity, and the resulting sodium and fluid removal, was evaluated in a preclinical study with 15 pigs (of which five had experimentally induced heart failure) and in a first-in-human single dose DSR proof-of-concept study (from which results are reported today). These studies demonstrated that DSR can result in the removal of large quantities of sodium and fluid in a safe and tolerable manner whilst having a negligible impact on the electrolyte concentrations in the bloodstream.

About Sequana Medical

Sequana Medical is a commercial stage medical device company focused on the development of innovative treatment solutions for the management of liver disease, heart failure, malignant ascites and other fluid imbalance disorders.

Sequana Medical's technology is based on its proprietary **alfa**pump platform, a fully implantable, programmable, wirelessly-charged, battery-powered system for automatic and continuous removal of fluid from the abdomen, which is applicable across multiple life-threatening disorders. The **alfa**pump is being

commercialised in Europe for the management of refractory ascites (chronic fluid build-up in the abdomen) due to liver cirrhosis and malignant ascites due to cancer. The number of patients with refractory liver ascites is forecast to increase dramatically due to the growing prevalence of NASH (Non-alcoholic Steatohepatitis).

Over 700 **alfa**pump systems have been implanted to date. The **alfa**pump has been endorsed by key independent third parties in Europe and has been included in the EASL (European Association for the Study of the Liver) clinical practice guidelines for decompensated cirrhosis, the German treatment guidelines (DGVS) for complications of liver cirrhosis and the U.K. NICE interventional procedure guidance for treatment of refractory ascites caused by cirrhosis. In January 2019, the U.S. FDA granted Breakthrough Device designation to the **alfa**pump for the treatment of recurrent or refractory liver ascites. The Company expects to start POSEIDON, the North American pivotal study, in the second half of 2019 to support approval of the **alfa**pump in recurrent or refractory liver ascites.

Sequana Medical has leveraged its **alfa**pump experience and is developing **alfa**pump DSR (Direct Sodium Removal) to deliver a convenient and fully implanted system for DSR therapy. Data from the first-in-human single dose DSR proof-of-concept study presented at Heart Failure 2019 demonstrated that DSR can result in the removal of large quantities of sodium and fluid in a safe and tolerable manner. The first clinical study of **alfa**pump DSR in patients with volume overload due to heart failure is expected to start in the second half of 2019.

Sequana Medical is headquartered in Ghent, Belgium. For further information, please visit www.sequanamedical.com.

Important Regulatory Disclaimers

*The **alfa**pump has not yet received regulatory approval in the U.S. and Canada. Any statement in this press release about safety and efficacy of the **alfa**pump does not apply to the U.S. and Canada because the device is currently undergoing clinical investigation in these territories.*

*DSR therapy is still in development and it should be noted that any statements in this press release regarding safety and efficacy arise from pre-clinical studies and ongoing clinical investigations which have yet to be completed. There is no link between DSR therapy and ongoing investigations with the **alfa**pump system in Europe, the U.S. and Canada.*

Forward-looking statements

This press release may contain predictions, estimates or other information that might be considered forward-looking statements. Such forward-looking statements are not guarantees of future performance. These forward-looking statements represent the current judgment of Sequana Medical on what the future holds, and are subject to risks and uncertainties that could cause actual results to differ materially. Sequana Medical expressly disclaims any obligation or undertaking to release any updates or revisions to any forward-looking statements in this press release, except if specifically required to do so by law or regulation. You should not place undue reliance on forward-looking statements, which reflect the opinions of Sequana Medical only as of the date of this press release.