PRESS RELEASE
REGULATED INFORMATION – INSIDE INFORMATION
18 October 2023, 07:00 am CEST

Sequana Medical announces initial positive data from MOJAVE, a US Phase 1/2a study of DSR® 2.0 for treatment of heart failure through breaking vicious cycle of cardiorenal syndrome

- **First two US patients from non-randomized cohort successfully treated with DSR 2.0**
- **Initial data indicate that DSR 2.0 is safe and well tolerated, restores diuretic response and improves cardiorenal status**
- **Biomarker analysis from RED DESERT and SAHARA studies supports DSR mechanism of action as breaking vicious cycle of cardiorenal syndrome (CRS)**
- **Start of randomized cohort of up to 30 US patients planned for Q1 2024 following DSMB[i] review**

Conference call with live webcast by Sequana Medical tomorrow, 19 October 2023 at 03:00 pm CEST / 09:00 am EST

Ghent, Belgium – 18 October 2023 – Sequana Medical NV (Euronext Brussels: SEQUA) (the "**Company**" or "**Sequana Medical**"), a pioneer in the treatment of fluid overload in liver disease, heart failure and cancer, today announces that the first two patients from the non-randomized cohort of the MOJAVE study were successfully treated with DSR 2.0, including safe and effective maintenance of euvolemia without the need for loop diuretics, considerable benefit in their cardiorenal status and a dramatic improvement in their diuretic response and loop diuretic requirements. Detailed biomarker analysis of the preceeding RED DESERT and SAHARA trial patients indicates DSR mechanism of action as breaking the vicious cycle of cardiorenal syndrome.

Dr. Jeffrey Testani, Associate Professor at Yale University and Heart Failure Scientific Advisor to Sequana Medical, commented: *"Cardiorenal syndrome is an area of key unmet clinical need in heart failure with complex, vicious cycle of negative interactions between the heart and the kidney. Based on extensive biochemical analysis, DSR appears to have the potential to interupt this vicious cycle of disease through effectively managing congestion while avoiding the widely appreciated negative effects on CRS from loop diuretics, resulting in improved cardiorenal status. This is highly encouraging and together with the positive initial data from MOJAVE, indicates the potential for DSR therapy as a promising treatment for diuretic-resistance and cardiorenal syndrome in heart failure."*

Dr. Oliver Gödje, Chief Medical Officer of Sequana Medical, commented: *"We are pleased that the first two patients ever treated with DSR in the US were enrolled smoothly and continue to show similar beneficial effects of DSR therapy as seen in RED DESERT and SAHARA. We are confident that after the third patient is treated and based on these favorable results, the multi-centric roll-out in Q1 2024 will start as planned and expect that DSR will demonstrate its full benefits compared to the loop diuretic control group. We are excited about the potential for DSR in cardiorenal syndrome where there is a clear need for improved therapeutic options."*

Positive interim data from non-randomized cohort of MOJAVE study

The first two patients treated in the non-randomized cohort of the MOJAVE study had heart failure with preserved ejection fraction (HFpEF) and severe diuretic resistance at baseline (mean furosemide equivalent dose of respectively 1,280 and 800 mg per day). At the start of the study treatment period, loop diuretics were withheld, and patients were treated with DSR 2.0 up to daily for four weeks.

After the four-week DSR treatment period, both patients maintained euvolemia without the need of loop diuretics and showed improved cardiorenal status. Their diuretic response[ii] nearly normalized with a mean increase of 454% in their six-hour urinary sodium excretion versus baseline. These interim data also show a broad improvement in their kidney function with an improvement in eGFR[iii], as well as blood urea nitrogen[iv] post-treatment vs baseline. Since both patients had HFpEF, their NT-proBNP[v] levels were within normal ranges at baseline and were maintained post-treatment, indicating that their stable cardiovascular status was preserved.

Difference 4-week post treatment vs baseline	Patient 1	Patient 2
Increase in 6-hour mmol sodium excretion	+195%	+712%
Decrease in blood urea nitrogen	-65%	-52%
Increase in eGFR	+64%	+49%

To date, no clinically relevant changes in serum sodium levels or progressive hyponatremia were observed and no serious adverse events occurred, indicating that DSR 2.0 was safe and well tolerated in these first two US patients.

Both patients are currently in the follow-up period without any loop diuretics (since commencing DSR therapy, the first patient is 9.5 weeks off loop diuretics and the second patient is 4 weeks off loop diuretics). The third patient in the non-randomized cohort has been enrolled and will have completed DSR treatment and initial follow-up before year end. An independent Data and Safety Monitoring Board (DSMB) meeting to review the data from the three patients in the non-randomized cohort is planned in early Q1 2024 to approve the start of the randomized cohort, planned for Q1 2024.

Breaking the vicious cycle of cardiorenal syndrome (CRS)

Cardiorenal syndrome is a key clinical challenge in heart failure and results from the combined vicious cycle of dysfunction of the heart and kidney with hypothesised complex and interconnected mechanisms such as aberrations in hemodynamic, neurohormonal, inflammatory, and sodium handling pathways. Despite the complex multidimensional pathophysiology, the resultant clinical profile is thought to manifest as a self-reinforcing negative feedback cycle characterized by decreased glomerular filtration, increased renal sodium avidity, and congestion, despite escalating diuretic doses.

No current therapies have been shown to improve patient outcomes in this complex and poorly understood indication. Reducing congestion is a key element of therapy but loop diuretics exacerbate many of the core mechanisms thought to underly CRS, thus even worsening diuretic resistance and CRS. Through effective

control of the volume status for an extended period of time and thereby avoiding the negative consequences of loop diuretics, DSR has the potential to break the negative feedback cycle of this important indication with clear unmet clinical needs.

Extensive analysis of validated biomarkers from patients in the RED DESERT and SAHARA studies shows the benefit from DSR therapy on i) volume status, ii) normalized diuretic response and dramatically reduced loop diuretic dosing, iii) improvement in kidney function, iv) neurohormonal status and signalling, as well as v) cardiovascular parameters. As previously disclosed, in these patients there were no congestion-related re-hospitalizations, a one class improvement in their NYHA[vi] status and a reduction of 75% in their predicated one-year mortality (based on the Seattle Heart Failure model).

Data from the RED DESERT and SAHARA proof-of-concept studies have been submitted for publication in a peer-reviewed journal. The Company will update the market as soon as it is published.

Details Conference Call and Webcast by Sequana Medical

Sequana Medical management will host a conference call with a live webcast presentation **tomorrow 19 October 2023** at 03:00 pm CEST / 09:00 am EST.

- Registration webcast: please click here
- Registration conference call (only if you wish to participate in the Q&A): please click here. Once registered, you will receive dial-in numbers and a confirmation code.

The webcast and conference call will be conducted in English and a replay will be available on Sequana Medical's website shortly after.

For more information, please contact:

Sequana Medical

Lies Vanneste
Director Investor Relations
E: IR@sequanamedical.com
T: +32 (0)498 053579

About the MOJAVE study

MOJAVE is a randomized controlled multi-center Phase 1/2a study in the US to evaluate the safety and efficacy of DSR 2.0, Sequana Medical's second-generation DSR product (administered via a peritoneal dialysis (PD) catheter), in diuretic-resistant chronic heart failure patients with persistent congestion. The objective is to validate the positive results from the RED DESERT and SAHARA studies in US patients using DSR 2.0.

The study has started with a non-randomized cohort of three patients treated with DSR 2.0 on top of optimized usual care for congestive heart failure for up to four weeks, followed by a three-month safety follow-up period

(with an initial review after 30 days). Following review and approval of the non-randomized cohort data by the independent Data and Safety Monitoring Board (DSMB) planned for early Q1 2024, up to a further 30 patients will be enrolled in the multi-center randomized cohort. The intention is for up to 20 patients to be treated with DSR 2.0 on top of optimized usual care for congestive heart failure for up to four weeks, and for up to ten patients treated with intravenous loop diuretics alone as part of maximized usual care for congestive heart failure.

Primary and secondary safety and efficacy endpoints include the rate of adverse and serious adverse events and the improvement in diuretic response (measured as a six-hour urine sodium output) from baseline through the end of the treatment period. Exploratory endpoints measured from baseline through the end of the treatment period include change in weight (volume status), creatinine (a marker of renal function), natriuretic peptides (a marker of heart failure) and New York Heart Association (NYHA) functional class; and the number of heart failure related rehospitalizations.

About Sequana Medical

Sequana Medical NV is a pioneer in treating fluid overload, a serious and frequent clinical complication in patients with liver disease, heart failure and cancer. This causes major medical issues including increased mortality, repeated hospitalizations, severe pain, difficulty breathing and restricted mobility that severely impacts daily life. Although diuretics are standard of care, they become ineffective, untolerable or exacerbate the problem in many patients. There are limited effective treatment options for these patients, resulting in poor clinical outcomes, high costs and a major impact on their quality of life. Sequana Medical is seeking to provide innovative treatment options for this large and growing "diuretic-resistant" patient population. **alfa**pump® and DSR® are Sequana Medical's proprietary platforms that work with the body to treat diuretic-resistant fluid overload, delivering major clinical and quality of life benefits for patients and reducing costs for healthcare systems.

The Company has reported positive primary and secondary endpoint data from the North American pivotal POSEIDON trial of the **alfa**pump in recurrent or refractory ascites due to liver cirrhosis and is on track to file a Pre-Market Approval (PMA) application with the FDA in Q4 2023.

The Company has commenced MOJAVE, a US randomized controlled multi-center Phase 1/2a clinical trial of DSR 2.0 seeking to confirm the strong efficacy seen in the RED DESERT and SAHARA studies. The first two patients have been successfully treated with DSR 2.0, and top-line data from all of the first three patients is expected by year end. Sequana Medical recently reported that detailed biomarker analysis of RED DESERT and SAHARA patients indicates DSR's mechanism of action as breaking the vicious cycle of cardiorenal syndrome.

Sequana Medical is listed on Euronext Brussels (Ticker: SEQUA.BR) and headquartered in Ghent, Belgium. For further information, please visit www.sequanamedical.com.

Important Regulatory Disclaimers

*The **alfa**pump® system is currently not approved in the United States or Canada. In the United States and Canada, the **alfa**pump system is currently under clinical investigation (POSEIDON Trial) and is being studied in adult patients with refractory or recurrent ascites due to liver cirrhosis. DSR® therapy is still in development and it should be noted that any statements regarding safety and efficacy arise from ongoing pre-clinical and 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 United States or Canada.*

*Note: **alfa**pump® and DSR® are registered trademarks.*

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.

[i] DSMB: Data Safety Monitoring Board
[ii] Diuretic response assessed by 6-hour excretion of sodium after IV administration of 40mg furosemide
[iii] eGFR: estimated Glomerular Filtration Rate, a measure of kidney function
[iv] Blood urea nitrogen is a waste product normally cleared by the kidneys
[v] NT-proBNP: N-terminal pro B-type natriuretic peptide, a key cardiac function parameter
[vi] NYHA: New York Heart Association classification (data collected outside study protocols of RED DESERT and SAHARA)