Strong data from DSR® proof-of-concept studies in heart failure published in European Journal of Heart Failure

Serial Direct Sodium Removal in Patients with Heart Failure and Diuretic Resistance

Ghent, Belgium – 3 April 2024 – 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 results from two proof-of-concept studies, RED DESERT and SAHARA, of the Company's DSR therapy in patients with diuretic-resistant heart failure have been published in the prestigious peer-reviewed journal European Journal of Heart Failure[i]. The publication can be accessed here.

Dr. Jeffrey Testani, Associate professor at Yale University and senior author of the publication commented: *"Cardiorenal syndrome is a major clinical challenge in heart failure with a clear unmet need for therapies to effectively and durably address congestion and cardio-renal dysfunction. Currently the mainstay of therapy for sodium avidity and congestion are the loop diuretics, which actually worsen sodium avidity and cardiorenal syndrome. In the RED DESERT and SAHARA studies, patients' loop diuretics were completely replaced by DSR therapy for several weeks, resulting in an improvement in a multitude of metrics of cardiorenal health and a dramatic and durable improvement in their diuretic responsiveness and chronic loop diuretic requirements. This data is truly revolutionary, representing really the first and only novel therapeutic approach to treat diuretic resistance and cardiorenal syndrome in heart failure."*

Ian Crosbie, Chief Executive Officer of Sequana Medical, added: *"We are delighted with Dr. Testani's publication highlighting DSR as a potential treatment for cardio-renal syndrome, highlighting the need to break the vicious cycle of loop diuretic therapy. Diuretic-resistant heart failure and cardiorneal syndrome are large and growing markets both in the US and rest of world, with the clear need for novel treatments that can improve clinical outcomes beyond loop diuretics. We believe DSR's ability to virtually eliminate the need for loop diuretics for many months post-treatment represents a breakthrough in treatment options, and address one of the leading drivers of healthcare costs."*

In total, 18 patients with heart failure on high dose oral loop diuretics were enrolled in the RED DESERT and SAHARA clinical studies and received DSR therapy for up to four and six weeks respectively, whilst their loop diuretics were withheld. Data from these studies indicated that DSR could i) safely, effectively and rapidly eliminate fluid overload and restore euvolemia without the need of any loop diuretics; ii) deliver a considerable benefit in patients' cardiorenal health; and iii) deliver a dramatic and sustained improvement in diuretic responsiveness, thereby dramatically reducing the need for oral loop diuretics for many months post-therapy. In both RED DESERT and SAHARA studies, there were no congestion-related hospital readmissions, all patients improved their NYHA status by at least one class, and and the clinical benefits observed in the clinical studies resulted in a 75% reduction in predicted one-year mortality of patients pre- vs. post-intensive DSR therapy based on the Seattle Heart Failure Model.

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About DSR, a disease-modifying heart failure drug therapy tackling 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. Despite the complex 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. 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 clinical challenge.

Extensive analysis of 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. In these patients there were no congestion-related re-hospitalizations, a one class improvement in their NYHA status and a reduction of 75% in their predicated one-year mortality (based on the Seattle Heart Failure model). Initial data from the non-randomized cohort in the US MOJAVE study support these findings and indicated that DSR is safe and well tolerated, restores diuretic response and improves cardio-renal health.

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. Although diuretics are standard of care, they become ineffective, untolerable or exacerbate the problem in many patients. There are limited effective treatment options, 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's Premarket Approval (PMA) application for the **alfa**pump was submitted to the US FDA in December 2023 and accepted for substantive review in January 2024, having reported positive primary and

secondary endpoint data from the North American pivotal POSEIDON study in recurrent or refractory ascites due to liver cirrhosis.

Results of the Company's RED DESERT and SAHARA proof-of-concept studies in heart failure support DSR's mechanism of action as breaking the vicious cycle of cardiorenal syndrome. All three patients from the non-randomized cohort of MOJAVE, a US randomized controlled multi-center Phase 1/2a clinical study, have been successfully treated with DSR, resulting in a dramatic improvement in diuretic response and virtual elimination of loop diuretic requirements. The independent Data Safety Monitoring Board approved the start of the randomized MOJAVE cohort of up to a further 30 patients, which is planned after **alfa**pump US PMA approval.

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] Impact factor (2022) for European Journal of Heart Failure (EJHF) is 18.2. EJHF publishes reviews and editorials to improve the understanding, prevention, investigation and treatment of heart failure, including molecular and cellular biology, pathology, physiology, electrophysiology, pharmacology, as well as clinical, social and population sciences.