PRESS RELEASE
REGULATED INFORMATION – INSIDE INFORMATION
19 July 2022, 07:00 am CEST

Sequana Medical completes enrollment in Phase 2a SAHARA I DSR study, reports disease-modifying profile for Short Term DSR and provides business update

DSR (Direct Sodium Removal) heart failure drug development:

- **Completed enrollment in SAHARA I[i] with first-generation DSR product ("DSR 1.0") – extending study with second-generation DSR product ("DSR 2.0") to support US IND[ii] filing by year end**
- **Proof-of-concept delivered in diuretic-resistant heart failure patients with dramatic and durable improvements in validated clinical measures**
- **Heart failure disease-modifying profile – safe, rapid and effective decongestion with no congestion-related heart failure re-hospitalizations observed**
- **Clinical outcomes from RED DESERT and SAHARA result in a 75% reduction in predicted one-year mortality based on Seattle Heart Failure model[iii]**
- **Heart failure development program to focus on Short Term DSR with DSR 2.0**

alfapump® in North America:

- **Submission of Premarket Approval (PMA) to the US FDA expected in H2 2023**

Webcast and conference call for investors/analysts today at 3:00 pm CEST / 9:00 am ET

Ghent, Belgium – 19 July 2022 – Sequana Medical NV (Euronext Brussels: SEQUA) (the "**Company**" or "**Sequana Medical**"), a pioneer in the treatment of drug-resistant fluid overload in liver disease and heart failure, today announces the completion of enrollment in its Phase 2a SAHARA proof-of-concept study using its first-generation DSR product ("**DSR 1.0**") as treatment for congestive heart failure. Sequana Medical intends to extend SAHARA to treat a small number of patients with its proprietary second-generation DSR product ("**DSR 2.0**") to support the US IND filing, expected by year end.

The Company has conducted two proof-of-concept studies, the RED DESERT study in euvolemic heart failure patients and the SAHARA study in decompensated heart failure patients, demonstrating that intensive DSR therapy with DSR 1.0 delivers compelling and durable clinical improvements in diuretic-resistant heart failure patients, including safe, rapid and effective decongestion, dramatic improvement in cardio-renal status and restoration of diuretic responsiveness. As a result of the strong, durable clinical signals observed, the Company will focus the heart failure development program on Short Term DSR with its proprietary DSR 2.0 administered with a peritoneal catheter.

Ian Crosbie, Chief Executive Officer of Sequana Medical, said: *"We are very encouraged by the results from our DSR program and consider Short Term DSR to be a disease-modifying drug therapy for this large and very difficult-to-treat patient population. Based on what we have learned from RED DESERT and SAHARA, we will focus on Short Term DSR using our proprietary DSR 2.0. With just three to four weeks of DSR treatment, we*

believe that we can bring patients important clinical benefits lasting up to a year and progress this potential breakthrough therapy to patients in need as efficiently as possible."

Dr. Oliver Gödje, Chief Medical Officer at Sequana Medical, added: *"We and our advisors are very impressed by the results and see DSR therapy as a treatment for heart failure that is complementary to other therapies. As cardiologists, we struggle to remove congestion from patients with diuretic resistance, which is the primary driver of morbidity and hospitalization in heart failure. DSR therapy tackles the key clinical need of sodium overload in patients in whom loop diuretics are no longer effective. The patients treated with DSR therapy in our studies have not been re-hospitalized for congestion-related heart failure problems during their study follow-up period and the clinical outcomes resulted in a substantial increase in predicted survival using the Seattle Heart Failure Model. We are now preparing for a US IND filing of our DSR 2.0 by year end to start MOJAVE, our Phase 1b/2a US study."*

DSR heart failure drug development

Twelve decompensated diuretic-resistant heart failure patients have been enrolled in the SAHARA study using DSR 1.0. Interim results from ten evaluable[iv] patients after completion of the intensive DSR period demonstrated that DSR therapy safely, effectively and rapidly eliminated persistent congestion and restored euvolemia (i.e., normal amount of body fluids), resulting in a mean weight loss of 6kg. There was a near normalization of diuretic response with six-hour excretion of sodium more than doubling vs. baseline, as well as a considerable improvement in cardio-renal health, with a mean reduction in NT-proBNP, a key cardiac function parameter, of more than 30% vs. baseline and a stable renal function (eGFR[v]) vs. baseline despite this dramatic fluid loss. The need for loop diuretics was dramatically reduced for many months following completion of the intensive DSR therapy (see table below), which the Company believes is an important demonstration of the improvement in cardio-renal health of these patients.

Evaluable patient	# months follow-up post intensive DSR period	Reduction in diuretic dose
01-01	11	**90%**
01-03	8	**100%**
01-04	7	**90%**
01-05	8	**100%**
01-06	7	**100%**
01-08	6	**100%**
01-09	4	**83%**
01-10	6	**95%**
01-11	2	**97%**
01-12	2	**100%**

Additionally, patients treated with DSR therapy in both RED DESERT and SAHARA experienced no congestion-related heart failure hospital re-admissions during their follow-up period in the study. The clinical benefits observed in RED DESERT and SAHARA result in a 75% reduction in predicted one-year mortality of patients pre- vs. post-intensive DSR therapy based on the Seattle Heart Failure Model.

Based on the SAHARA observations, which reinforce those observed in the RED DESERT study, the Company believes that an intensive treatment period of three to four weeks of DSR therapy is sufficient for six to twelve months of important clinical benefits. Therefore the Company is focusing its DSR development program on Short Term DSR using its proprietary DSR 2.0 that is expected to have an improved therapeutic and favourable safety profile, adminstered via a peritoneal catheter. In addition, the Company believes that given Short Term DSR will be regulated as a drug only (rather than a drug-device combination for Long Term **alfa**pump DSR), this will shorten and derisk the clinical and regulatory paths, and therefore the time to market.

To support the US IND filing of DSR 2.0, the Company intends to extend SAHARA to treat a small number of patients with DSR 2.0. Patients with diuretic-resistant congestive heart failure on high doses of loop diuretics will undergo intensive DSR therapy with DSR 2.0 for two weeks which can be repeated up to two times depending on their euvolemic state, diuretic response and stable DSR dosing. Primary endpoints include safety and tolerability of DSR 2.0 and secondary feasibility endpoints include the ability of DSR therapy to restore and maintain euvolemia without the need for additional loop diuretic treatment. Top-line results of SAHARA, using DSR 1.0 and 2.0, and the US IND filing of DSR 2.0 are expected by year end.

To support a compelling package for partnering, the Company is expanding its planned MOJAVE US Phase 1b/2a study. This randomized controlled study in approximately 30 diuretic resistant chronic heart failure patients will evaluate Short Term DSR with DSR 2.0 administered via a peritoneal catheter on top of standard-of-care therapy vs. standard-of-care therapy alone. This study will commence following submission and approval of the US IND.

Update on **alfa**pump development in North America

POSEIDON, the North American pivotal study of the **alfa**pump in recurrent and refractory ascites due to liver cirrhosis is on track to report primary endpoint data in Q4 2022. Based upon recent FDA feedback, the biocompatibility testing to support the PMA submission has been extended by 3 months. The Company now plans to submit the PMA regulatory filing in the second half of 2023.

Webcast and Conference Call

Sequana Medical will host a webcast and conference call today at 03:00 pm CET / 09:00 am ET.

- 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.

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About fluid overload in heart failure (AKA congestion)

Heart failure is the leading cause of US hospitalizations in patients over 65 years old and 90% of these admissions are due to fluid overload, which is recognized as the primary driver of morbidity and hospitalization. Standard of care includes treatment with diuretic drugs, but these have well recognized toxicity and resistance issues. Half of the heart failure patients admitted for fluid overload are discharged with no clinically relevant loss of fluid and one in four is re-admitted to the hospital within 30 days of discharge. It is estimated that 200,000 US heart failure patients have drug-resistant congestion requiring repeated hospitalization, severely impacting their survival and quality of life and creating a heavy financial burden.

About DSR® (Direct Sodium Removal) in heart failure

Sequana Medical considers its' proprietary DSR to be a disease modifying therapy for heart failure. Fluid accumulation in heart failure patients is caused by the retention of too much sodium. The DSR drug-based

approach directly tackles this key clinical problem of sodium overload, and works in partnership with the kidneys to safely and rapidly eliminate the excess fluid. Complementary to existing heart failure therapies, clinical proof-of-concept studies using the Company's first-generation DSR product ("DSR 1.0") have shown that DSR can i) safely, effectively and rapidly eliminate fluid overload in heart failure patients, ii) improve the health of the heart and preserve renal function, and iii) restore the ability of the kidney to manage the fluid and sodium naturally, resulting in a large and long-lasting reduction in the need for diuretic drugs. In DSR treated patients, there have been no congestion-related re-hospitalizations during the study follow-up period 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[iii]. Top-line results of the Phase 2a SAHARA study using DSR 1.0 and the Company's proprietary second-generation DSR product ("DSR 2.0") are expected by year end, followed by the start of a Phase 1b/2a US efficacy study with DSR 2.0.

About Sequana Medical

Sequana Medical NV is a pioneer in treating drug-resistant fluid overload, a serious and frequent clinical complication in patients with liver disease and heart failure. Fluid overload is a well-recognized problem in these growing diseases, causing severe problems for the large number of patients for whom current medicines are no longer effective. These patients can have up to 15 liters of extra fluid in their bodies, causing major medical issues including increased mortality, repeated hospitalizations, severe pain, difficult breathing and restricted mobility that severely impacts daily life.

alfapump® and DSR® are Sequana Medical's proprietary approaches that work with the body to remove this excess fluid, delivering major clinical and quality of life benefits for patients and reducing costs for healthcare systems. 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 not currently approved in the United States or Canada. In the United States and Canada, the **alfa**pump system is currently under clinical investigation (POSEIDON Study) and is being studied in adult patients with refractory or recurrent ascites due to cirrhosis. For more information regarding the POSEIDON clinical study see www.poseidonstudy.com. 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. DSR® therapy is not currently approved for clinical research in the United States or Canada. There is no link between the DSR® therapy and ongoing investigations with the **alfa**pump system in Europe, the United States or Canada.*

***Note: alfa**pump® is a registered trademark. DSR® and **alfa**pump DSR® are registered trademarks in the Benelux, China, the EU, United Kingdom, and Hong Kong.*

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] SAHARA I: SAHARA study using DSR 1.0
[ii] IND: Investigational New Drug
[iii] Predicted one-year survival analysis using Seattle Heart Failure Model of seven patients from RED DESERT and eight patients from SAHARA pre- and post-intensive DSR therapy. Analysis includes physician-assessed data collected *post hoc*.
[iv] Of the 12 enrolled patients, one patient died due to a cardiac arrest three days after study initiation and for one patient the study protocol was not correctly applied
[v] eGFR: estimated Glomerular Filtration Rate