PRESS RELEASE
REGULATED INFORMATION – INSIDE INFORMATION
11 May 2021, 07:00 am CEST

Sequana Medical announces strong top-line results from RED DESERT alfapump DSR® study and expansion of DSR® development programme

- **RED DESERT data of all patients confirm:**
  - **alfa**pump **DSR is highly effective at managing fluid and sodium balance in diuretic-resistant heart failure patients without need for loop diuretics**
  - **restoration of diuretic response and improvement in cardio-renal function**
  - **improvement in diuretic response maintained in long-term follow-up**
- **SAHARA DESERT study in heart failure patients with residual congestion to start in Q2 2021**
- **Expanding DSR development programme with short-term DSR therapy**
- **Evaluating opportunity for DSR therapy for fluid and sodium removal in renal disease**

Conference call with live webcast today at 15:00 CEST / 09:00 am EDT

Ghent, BELGIUM – 11 May 2021 – Sequana Medical NV (Euronext Brussels: SEQUA), an innovator in the treatment of diuretic-resistant fluid overload in liver disease, malignant ascites and heart failure, today announces positive top-line results from the RED DESERT study with repeated dose **alfa**pump DSR® (Direct Sodium Removal) therapy in diuretic-resistant heart failure patients.

SAHARA DESERT, the study of the **alfa**pump DSR in diuretic-resistant heart failure patients with residual congestion is on track to start before the end of this quarter, with interim results expected before year-end and top-line results expected in H2 2022.

In addition, Sequana Medical announces that it will expand its DSR development program with the addition of short-term DSR therapy. Short-term DSR is expected to achieve faster adoption of DSR therapy by the clinical community, support **alfa**pump DSR market entry, expand the potential market opportunity and target earlier entry into the U.S. market. MOJAVE DESERT, the first U.S. feasibility study of short-term DSR therapy, is planned to start in H2 2022. Based on FDA feedback, SONORAN DESERT, the U.S. efficacy study of **alfa**pump DSR therapy, is now planned to commence in mid-2023 to allow completion of long-term pre-clinical studies.

Fluid and sodium overload is an important clinical problem in renal disease / hemodialysis and Sequana Medical is evaluating the opportunity for DSR therapy to improve clinical outcomes and is supporting the clinical work of Dr. McIntyre of Lawson Health Research Institute, Ontario, Canada.

Ian Crosbie, Chief Executive Officer at Sequana Medical, commented: "These RED DESERT results are very exciting and further confirm the potential clinical benefits of our **alfa**pump DSR therapy. Repeated **alfa**pump DSR therapy not only managed the fluid and sodium balance throughout the study without the need of any loop diuretics but crucially it also restored patients' diuretic response and overall cardio-renal status. We are

very encouraged by the durability of the reduction in loop diuretics and believe our novel **alfa**pump DSR therapy has the potential to transform the treatment of this large and growing patient group.

"In light of the success of RED DESERT, we have concluded the study at eight patients so that we can move on to the SAHARA DESERT study as soon as possible, where we will be treating our anticipated patient population.

"We are expanding our DSR development programme into short-term DSR treatment, complementing our long-term **alfa**pump DSR treatment. We believe that short-term DSR therapy plays a crucial role in establishing this breakthrough treatment and enhances the market opportunity for **alfa**pump DSR therapy. This combined strategy of short-term and long-term DSR therapy will reinforce our leadership role in addressing diuretic-resistant fluid overload."

Strong top-line results from RED DESERT

Eight patients diagnosed with stable chronic heart failure on high dose oral diuretics (mean furosemide equivalent dose of 323 mg/day) were implanted with the **alfa**pump DSR system and underwent up to six weeks of DSR therapy whilst their loop diuretic treatment was withheld. The heart failure patients enrolled in the study had an overall high disease severity at baseline, including a mean left ventricular ejection fraction of 24% and mean NT-proBNP of 4,589 pg/mL.

During the course of the six-week therapy, none of the patients required any loop diuretics, demonstrating the ability of repeated **alfa**pump DSR therapy to effectively manage their fluid and sodium balance. After the six-week study, the mean response to a standard diuretic challenge (40 mg intravenous furosemide) improved by more than 250% ($p<0.001$ vs baseline, N=7) as measured by the six-hour excretion of sodium. This improvement of diuretic efficiency was maintained with a 79% reduction of average loop diuretic dose at a median of 10 months post-study versus baseline and all patients were receiving less than or equal to 50% of their baseline diuretic dose (maximum follow-up post-study is 12.5 months).

The results clearly show a significant benefit to the cardio-renal function of these patients with a mean 30% reduction in NT-proBNP ($p<0.001$ vs baseline, N=7), mean 22% improvement in estimated glomerular filtration rate ($p<0.001$ vs baseline, N=7) and mean 22% reduction in creatinine ($p<0.001$ vs baseline, N=7). Typically, managing the fluid balance in these patients through aggressive diuretic use would be associated with declining cardio-renal function, whilst RED DESERT showed that both of these functions were improved following repeated **alfa**pump DSR therapy.

In all patients, there were no clinically relevant changes in serum sodium levels or progressive hyponatremia. There were two serious adverse events in two of the last three patients, both having advanced heart failure. There was one transient ischemic attack (fully recovered) and one sudden cardiac death. The Data Monitoring Committee (DMC) assessed both events as possibly related to the study therapy or procedure but unlikely to be related to the device. The site Principal Investigator assessed that neither event was related to the study therapy, procedure or device.

Dr. Jozef Bartunek, Interventional Cardiologist at Onze-Lieve-Vrouw Hospital in Aalst (Belgium) and Principal Investigator of the RED DESERT study, commented: "These results confirm that **alfa**pump DSR therapy is well tolerated and manages to quickly maintain a neutral sodium balance and stable body weight over six weeks, despite complete withdrawal of loop diuretics. The substantial improvement in diuretic response together with the meaningful improvement in NT-proBNP and renal function could be a potential game-changer."

Dr. Jeffrey Testani, Associate Professor at Yale University and Heart Failure Scientific Advisor of Sequana Medical, added: "There is a significant need for novel therapies for sodium and fluid removal in heart failure, given the toxicity of loop diuretics and the high prevalence of resistance to these agents. The simultaneous normalisation of diuretic response and improvement in cardio-renal status of the RED DESERT patients is a never before seen treatment effect and could translate into important long-term clinical benefits in heart failure patients. I am looking forward to further clinical research to better understand the cardio-renal benefits of **alfa**pump DSR therapy and its application to heart failure patients in urgent need of improved treatment options."

SAHARA DESERT on track to start before end Q2 2021 – Interim results end 2021, Top-line results H2 2022

The SAHARA DESERT study will build on the learnings from RED DESERT and moves into sicker heart failure patients - those with residual congestion and for whom oral diuretics are no longer effective at preventing fluid overload. The study in 20 patients will evaluate the treatment algorithm and the ability of **alfa**pump DSR therapy to eliminate the residual congestion and restore the correct fluid status (euvolemia) for up to 22 weeks. Interim results are expected before end 2021 with top-line results planned for H2 2022.

Expanding DSR development programme with short-term as well as long-term DSR therapy

As a result of the positive results from RED DESERT, the DSR development programme is being expanded into short-term DSR therapy to complement long-term **alfa**pump DSR therapy. The intention is to enable faster adoption of DSR therapy by the clinical community by reducing barriers to adoption, support **alfa**pump DSR market entry, expand the potential market opportunity and target earlier entry into the U.S. market.

A key element of the DSR programme is the development of DSR Infusate 2.0, Sequana Medical's proprietary DSR Infusate. The intention is to deliver an infusate with a superior therapeutic profile as well as a high margin recurring revenue flow to accompany **alfa**pump sales. Pre-clinical development work on DSR Infusate 2.0 is ongoing and preparations are being made for Chemistry, Manufacturing and Controls (CMC) activities.

Short-term DSR therapy will involve repeated DSR treatment for approximately 2 weeks, using DSR Infusate 2.0 in combination with a peritoneal catheter (instead of the **alfa**pump). MOJAVE DESERT, the U.S. proof-of-concept study of short-term DSR therapy is scheduled to start in H2 2022. The study design will leverage the learnings from SAHARA DESERT as well as the anticipated superior therapeutic profile of DSR Infusate 2.0. The use of short-term DSR therapy without the **alfa**pump has been enabled by the fundamental DSR patents that have been granted in the U.S. and Europe, and are under review elsewhere in the world.

Following discussions with the FDA, SONORAN DESERT, the U.S. controlled efficacy study of **alfa**pump DSR is now planned to commence in mid-2023 to enable completion of long-term pre-clinical studies prior to study commencement.

Evaluating opportunity for DSR therapy in fluid and sodium overload in renal disease / hemodialysis

The effective management of fluid and sodium overload is a significant problem in renal disease / hemodialysis. Sequana Medical is evaluating the opportunity for DSR therapy to address this poorly met clinical need and is supporting the work of Dr. Chris McIntyre of the Lawson Health Research Institute, Ontario, Canada who is evaluating the use of DSR therapy in effective volume management and sodium removal in prevalent hemodialysis patients (ClinicalTrials.gov NCT04603014). Results of this work will be shared in due course.

Conference Call and Webcast

Sequana Medical will host a conference call with live webcast presentation today at 15:00 CEST / 09:00 EDT.

- 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
Tel: +32 498 05 35 79
Email: IR@sequanamedical.com

LifeSci Advisors
Guillaume van Renterghem
Tel: +41 76 735 01 31
Email: gvanrenterghem@lifesciadvisors.com

About RED DESERT study design

RED DESERT is a prospective, single-arm, first-in-human study to evaluate the safety and feasibility of **alfa**pump DSR. Eight patients diagnosed with stable chronic heart failure on high doses of oral diuretics were implanted with the **alfa**pump DSR system (**alfa**pump and implanted surgical port). Following implantation,

patients underwent a standardised diuretic challenge (40 mg intravenous furosemide) to quantify their response to diuretics, and this was repeated at specific time points throughout the study. At the start of the study treatment, patients were admitted for a 14-day in-patient period in which diuretics were withheld and patients were treated with DSR D10% infusate on Monday, Wednesday and Friday. Following the 14-day in-patient period, diuretics continued to be withheld and patients came into the clinic for their DSR treatment over the subsequent four weeks.

The primary safety endpoints include rate of device, procedure and/or therapy related serious adverse events through day 14 and through day 42. Secondary feasibility endpoints include the ability of **alfa**pump DSR to maintain a neutral sodium balance in the absence of diuretic treatment and the sustained effect of DSR to maintain euvolemia through week six. Additional exploratory endpoints include the potential impact of DSR to restore response to diuretics following DSR treatment. For more information about the study, please visit clinicaltrials.gov (NCT04116034).

About Sequana Medical

Sequana Medical is a commercial stage medical device company utilizing its proprietary **alfa**pump® and DSR® (Direct Sodium Removal) technologies to develop innovative treatments for fluid overload in liver disease, malignant ascites and heart failure where diuretics are no longer effective. Fluid overload is a frequent complication of many large diseases including advanced liver disease driven by NASH (non-alcoholic steatohepatitis)-related cirrhosis and heart failure, with diuretic resistance being widespread. The U.S. market for the **alfa**pump resulting from NASH-related cirrhosis is forecast to exceed €3 billion annually within the next 10-20 years. The heart failure market for DSR and the **alfa**pump DSR® is estimated to be over €5 billion annually in the U.S. and EU5 by 2026.

The **alfa**pump is a unique, fully implanted wireless device that automatically pumps fluid from the abdominal cavity into the bladder, where it is naturally eliminated through urination. DSR is Sequana Medical's proprietary approach to managing sodium and fluid overload through use of a sodium-free infusate administered into the abdominal cavity.

In the U.S., the Company's key growth market, the **alfa**pump has been granted breakthrough device designation by the FDA for recurrent or refractory ascites due to liver cirrhosis. Interim data from the ongoing North American pivotal study (POSEIDON) showed positive outcomes against all primary endpoints of the study. This study is intended to support a future marketing application of the **alfa**pump in the U.S. and Canada. In Europe, the **alfa**pump is CE-marked for the management of refractory ascites due to liver cirrhosis and malignant ascites and is included in key clinical practice guidelines. Over 850 **alfa**pump systems have been implanted to date.

Sequana Medical has combined its proven **alfa**pump and proprietary DSR therapy, and is developing the **alfa**pump DSR, a breakthrough approach to fluid overload due to heart failure. RED DESERT, the repeated dose **alfa**pump DSR study in diuretic-resistant heart failure patients has demonstrated that repeated DSR therapy is able to both manage the fluid and sodium balance of these patients as well as restore their diuretic

response and cardio-renal status.

Sequana Medical is 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. The 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. The 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.*

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.