PRESS RELEASE
REGULATED INFORMATION – INSIDE INFORMATION
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Sequana Medical announces DSMB approval to start randomized MOJAVE cohort – US Phase 1/2a study of DSR® 2.0 for treatment of heart failure

- **DSMB[i] rates DSR 2.0 as safe following review of data from non-randomized cohort**
- **Data from non-randomized cohort confirms dramatic improvement in diuretic response and at least 95% reduction in loop diuretic requirements up to almost four months after last DSR therapy**
- **First patient enrolled in randomized controlled cohort expected in Q1 2024**

Ghent, Belgium – 23 January 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 an independent Data and Safety Monitoring Board (DSMB) approved the start of the randomized cohort in MOJAVE, the US Phase 1/2a study of DSR 2.0 for treatment of patients with diuretic-resistant heart failure, following review of the safety data reported from the non-randomized cohort.

Follow-up data from the three patients in the non-randomized cohort confirm the durable improvement in their cardio-renal health and support DSR's mechanism of action as breaking the vicious cycle of cardiorenal syndrome.

The randomized controlled cohort will enrol up to 30 additional patients across different centers in the US, with up to 20 patients treated with DSR 2.0 on top of optimized usual care for congestive heart failure for up to four weeks, and up to ten control patients treated with intravenous loop diuretics as part of maximized usual care for congestive heart failure. After the last DSR treatment, patients will be followed for a three-month safety follow-up period. The first patient is expected to be enrolled in Q1 2024 and interim data are planned for H2 2024.

Dr. Oliver Gödje, Chief Medical Officer of Sequana Medical, commented: *"We are delighted to announce the ongoing progress of our US MOJAVE study and look forward to enrol the first patient in the randomized cohort later this quarter. Building upon the strong data reported from the non-randomized MOJAVE cohort and our previous RED DESERT and SAHARA studies, we are confident about the clinical effectiveness of our DSR therapy compared to loop diuretics. We look forward to reporting interim data from the MOJAVE randomized cohort in the second half of this year to further demonstrate the potential of DSR as a disease-modifying heart failure drug therapy tackling cardiorenal syndrome."*

Positive data from non-randomized cohort of MOJAVE study

Data from the four-week DSR treatment period, as reported previously[ii]:

All three 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 1,227 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, followed by a three-month safety follow-up period.

Dramatic improvement in diuretic response and renal status: During the four-week DSR treatment period, all three patients maintained euvolemia without the need of loop diuretics. Their diuretic response[iii] nearly normalized with a mean increase of 324% in their six-hour urinary sodium excretion post-treatment vs baseline. There was a broad improvement in their kidney function with a a mean improvement in eGFR[iv] of 47% and blood urea nitrogen[v] of 57% post-treatment vs baseline.

Updated data from the three-month safety follow-up period:

Loop diuretics virtually eliminated vs. baseline: Two patients have completed the three-month safety follow-up period and one patient is still in the follow-up period. The need for loop diuretics was dramatically reduced or even completely eliminated up to 15 weeks after the four-week DSR treatment period (see table below).

Patient	No. of weeks after last DSR therapy	Reduction in furosemide equivalent dose vs. baseline
1	15	**97%**
2	15	**100%**
3	9	**95%**

Improvement in renal parameters maintained: At the end of the three-month safety follow-up period, the diuretic response of the two patients who already completed the study remained normalized, with a similar high output in their six-hour urinary sodium excretion as compared to their dramatically improved diuretic response after the four-week DSR treatment period. Their kidney function also remained stable as measured by their improvement in eGFR and blood urea nitrogen.

To date, no clinically relevant changes in serum sodium levels or progressive hyponatremia were observed and none of the patients needed to be hospitalized for congestion since the start of the study. Until today, there was only one serious adverse event of short-term hypertension at 12 weeks after the last DSR therapy, which was adjudicated as non-related to DSR therapy. Short-term hypertension is often seen in this very sick patient population. These data indicate that DSR 2.0 is safe and well tolerated as confirmed by the DSMB.

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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 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 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). Data from these patients showed i) that DSR was safe and could effectively maintain euvolemia without the need for loop diuretics, ii) a considerable benefit in their cardio-renal health and iii) a dramatic improvement in their diuretic response and at least 95% reduction in loop diuretic requirements up to 15 weeks after the last DSR therapy. Following the positive review of the non-randomized cohort data by the independent Data and Safety Monitoring Board (DSMB) in January 2024, up to a further 30 patients will be enrolled in the multi-center randomized cohort. Up to 20 patients will be treated with DSR 2.0 on top of optimized usual care for congestive heart failure for up to four weeks, and up to ten control patients treated with intravenous loop diuretics 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 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 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 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.

Data from the RED DESERT and SAHARA proof-of-concept studies have been submitted for publication in a peer-reviewed journal.

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 submitted a Premarket Approval (PMA) application for the **alfa**pump to the US FDA in December 2023 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. MOJAVE, a US randomized controlled multi-center Phase 1/2a DSR clinical study is ongoing, seeking to confirm the strong efficacy seen in the RED DESERT and SAHARA studies. All three patients from the non-randomized cohort have been successfully treated with DSR and the DSMB approved the start of the randomized cohort of up to a further 30 patients.

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] See press release of 29 November 2023
[iii] Diuretic response assessed by 6-hour excretion of sodium after IV administration of 40mg furosemide