PRESS RELEASE
REGULATED INFORMATION – INSIDE INFORMATION
1 July 2021, 07:00 am CEST

Sequana Medical announces positive results from second interim analysis of North American pivotal alfapump® study (POSEIDON)

- **Interim data from 26 patients in the Roll-In Cohort reconfirm positive outcomes against all primary endpoints[i]**
    - **Over 90% reduction in mean frequency of therapeutic paracentesis versus baseline**
    - **All patients experienced at least 50% reduction in mean frequency of therapeutic paracentesis per month versus baseline**
    - **Clinically important improvement in quality of life maintained even up to 12 months post-implantation**
    - **Safety profile remains in line with expectations – three patients experienced a composite primary safety event.**
- **Primary endpoint read-out from POSEIDON Pivotal Cohort expected in Q3 2022**

Conference call with live webcast today at 14:00 CEST / 08:00 am EDT

Ghent, BELGIUM – 1 July 2021 – Sequana Medical NV (Euronext Brussels: SEQUA, the "Company" or "Sequana Medical"), an innovator in the treatment of diuretic-resistant fluid overload in liver disease, malignant ascites and heart failure, today announces positive results from the second interim analysis of POSEIDON, the North American pivotal study of the **alfa**pump for the treatment of recurrent or refractory ascites due to liver cirrhosis. These interim data from 26 patients in the Roll-In Cohort are in line with the previous interim data[ii], including positive outcomes against all primary endpoints of the study and a rapid and persistent clinically important improvement in quality of life measures.

The Company also announces that based on an analysis of attrition between study enrolment and **alfa**pump implantation, it is anticipated that approximately 10 additional patients will need to be enrolled in the Pivotal Cohort. Among other factors, COVID-19-related delays in elective surgery resulted in some enrolled patients in the Pivotal Cohort no longer meeting the inclusion criteria at the time of planned implantation. As a consequence, patient recruitment is now expected to complete in Q3 2021 (instead of Q2 2021) and reporting of the primary endpoint in Q3 2022 (instead of Q2 2022). Filing of the Pre-Market Approval (PMA) to the U.S. FDA remains planned for H2 2022.

Ian Crosbie, Chief Executive Officer at Sequana Medical, commented: "I'm delighted to see the results from this larger cohort of Roll-In patients reaffirming the previous positive efficacy results of the **alfa**pump and providing longer-term evidence of the reduction in therapeutic paracentesis and continued improvements in quality of life. While we anticipate the need to enroll additional patients due to higher attrition in the pre-implant observation period, this is a reflection of how the condition of these patients continues to deteriorate,

and underlines how important **alfa**pump can be to these patients. The last patients are expected to be enrolled over the next quarter, and we are looking forward to the rapid completion of POSEIDON."

Professor Florence Wong, University of Toronto, Hepatologist at Toronto General Hospital, Ontario, Canada and Principal Investigator for the POSEIDON study, commented: "Ascites imposes a heavy burden and devastating impact on patients' quality of life. These interim results further demonstrate that the **alfa**pump could provide great benefit to patients and help limit their visits to the hospital for paracentesis. The safety data are in line with expectations and reassuring for the potential of the **alfa**pump as a long-term treatment in this fragile patient population. I look forward to continuing to study the **alfa**pump and generating further data to reinforce its potential to address this significant unmet medical need."

Positive interim data of 26 patients from Roll-In Cohort

In this second interim analysis, 26 patients from the Roll-In Cohort (underlying etiology: 50% alcohol, 23% non-alcoholic steatohepatitis (NASH), 4% NASH-alcohol, 4% hepatitis C and 19% other/mixed etiology) were implanted with the **alfa**pump. Before enrolment, these patients required on average 3.8 Therapeutic Paracenteses (TP) per month, an indication that North American patients seem to have more TP per month compared to Europe. Data from this Roll-In Cohort substantially exceed the primary endpoints as defined for the Pivotal Cohort in the study, demonstrating a mean reduction of over 90% in the frequency of TP post-implant versus baseline and all patients having at least a 50% reduction in the mean frequency of TP per month[i].

The new quality of life data, assessed via established health-survey questionnaires SF36 (a general health quality survey) and Ascites Q (a questionnaire developed for patients with ascites) confirm the rapid positive impact of the **alfa**pump on patient's quality of life. Both, the mean physical component score of SF36 and the mean score of Ascites Q, show a clinically important improvement (exceeding the threshold for Minimal Clinically Important Difference) from baseline to 6 months post-implantation and the improvement in quality of life measures was maintained for up to 12 months post-implantation (n=6 patients at 12 months).

Safety profile is in line with expectations with no unanticipated adverse device effects (UADE[iii]) during the course of the study. Three out of the 26 Roll-In patients experienced a composite primary safety event as adjudicated by the Clinical Events Committee (CEC), including one patient who died due to an implant procedure-related event and the other two patients having the **alfa**pump explanted, one due to wound dehiscence and the other due to persistent hematuria after a car accident.

Primary endpoint data of Pivotal Cohort expected in Q3 2022

The POSEIDON study design includes a three-month observation period between study enrolment and **alfa**pump implantation for patients in the Pivotal Cohort. A detailed review of study enrolment, including an analysis of attrition between study enrolment and planned **alfa**pump implantation has identified a higher rate of attrition than forecast when the study was planned. The cause of this includes the number of patients whose **alfa**pump implantation was delayed for COVID-related matters and subsequently failed to meet re-evaluation of study inclusion / exclusion criteria prior to implantation, likely due to disease progression. The review concluded that approximately 10 additional patients will need to be enrolled in the Pivotal Cohort in order to implant up to 50 patients with the **alfa**pump following the three-month observation period.

Completion of patient enrolment is now expected in Q3 2021 instead of Q2 2021, with planned reporting of the primary endpoint in Q3 2022.

Conference Call and Webcast

Sequana Medical will host a conference call with live webcast presentation today at 14:00 CEST / 08:00 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.

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About the pivotal POSEIDON study

POSEIDON is a single-arm, open-label, within subject cross-over study of the **alfa**pump in patients with recurrent or refractory ascites due to liver cirrhosis and is being conducted in approximately 20 centres across the U.S. and Canada. Patients are being enrolled in the Pivotal Cohort, entering into the pre-implant observation period, allowing for up to 50 patients to be implanted with the **alfa**pump for primary endpoint analysis. The study allows for up to 30 patients to be enrolled in a Roll-In Cohort, to ensure centres are experienced with the **alfa**pump implantation prior to enrolment of patients in the Pivotal Cohort.

Pivotal Cohort patients will enter into a three month pre-implant observation period in which they will receive standard of care therapy (consisting of therapeutic paracentesis) before the **alfa**pump is implanted. Patients from the Roll-In cohort will immediately be implanted with the **alfa**pump. The primary effectiveness outcomes of the study include the proportion of patients with a 50% reduction in the overall average frequency of therapeutic paracentesis per month in the post-implant observation period (month four to month six after implantation) as compared to the pre-implant observation period. The primary safety endpoint is the rate of

alfapump related re-interventions adjudicated by the Clinical Events Committee. Patients will be followed for up to two years for analysis of secondary outcome measurements including safety (device and/or procedure-related adverse events), quality of life (assessed by general SF36 as well as disease-specific Ascites Q questionnaires), patients' nutritional status, health economics and overall survival. For more information about the study, please visit clinicaltrials.gov (NCT03973866).

About recurrent and refractory ascites

Ascites is a condition where excess fluid builds up in your abdomen. Ascitic fluid is a protein-containing fluid that leaks from the liver as a result of advanced liver cirrhosis. Patients may accumulate as much as 10 to 15 litres of ascitic fluid within the abdomen every 15 days. Patients suffering from recurrent or refractory ascites have limited treatment options and often have severely impacted quality of life due to the severe swelling of the abdomen, resulting in pain, difficulty breathing, moving, sleeping and eating, the development of various hernias and the risk for developing renal dysfunction. The number of patients with refractory liver ascites is expected to increase dramatically due to the growing prevalence of NASH (Non-Alcoholic Steatohepatitis)–related cirrhosis. Paracentesis is the mainstay in chronic clinical management of refractory ascites but it is an invasive procedure, requiring frequent hospitalisations, severely impacting patients' quality of life and provides only temporary benefit.

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 Roll-In Cohort of 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

alfapump 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 improve their cardio-renal status. The SAHARA DESERT study of **alfa**pump DSR in decompensated heart failure patients is ongoing.

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.

[i] Pre- and post-implant periods for this analysis of the Roll-In Cohort differ from those that will be used for the Pivotal Cohort analysis
[ii] Press release 19 November 2020
[iii] Unanticipated adverse device effect is any serious adverse effect on health or safety, any life-threatening problem or death caused by, or associated with a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the application; or any other unanticipated serious problem associated with a device that relates to the rights, safety, or welfare of subjects (source: www.fda.gov)