PRESS RELEASE
REGULATED INFORMATION – INSIDE INFORMATION
28 December 2023, 07:00 am CET

Sequana Medical submits Premarket Approval application to US FDA for alfapump® in recurrent or refractory ascites due to liver cirrhosis

Pending FDA approval, alfapump could become the first active implantable medical device in the US for treating liver ascites

Ghent, Belgium – 28 December 2023 – 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 it has submitted a Premarket Approval (PMA) application to the US Food and Drug Administration (FDA) for **alfa**pump, the Company's fully implantable, wirelessly charged device for patients with recurrent or refractory ascites due to liver cirrhosis. The **alfa**pump received breakthrough device designation from the US FDA in 2019.

Recurrent or refractory ascites is a severe condition characterized by the accumulation of fluid in the abdomen. The current standard treatment involves therapeutic paracentesis, an invasive and burdensome procedure that drains ascites from the abdomen using a large needle over an extended period. If approved by the FDA, the **alfa**pump could become the first active implantable medical device in the US that automatically and continuously removes ascites from the abdomen into the bladder, where it is naturally eliminated through urination.

Timur Resch, Global Vice President QM/QA/RA at Sequana Medical, commented: *"The submission of our Premarket Approval application to the FDA is the result of an enormous team effort and a clear demonstration of our intensive preparation to fulfil US regulatory requirements. We have great confidence in the strength of our PMA submission and look forward to work in close collaboration with the FDA to facilitate a seamless and thorough review process intended to bring our breakthrough device to the US market as soon as possible."*

Ian Crosbie, Chief Executive Officer of Sequana Medical, added: *"This is a key milestone for the **alfa**pump and underscores our commitment to improving treatment options for patients with recurrent or refractory liver ascites. This overlooked patient group is forecast to grow strongly due to NASH / MASH and today's limited treatment options often lead to poor clinical outcomes, severely reduced quality of life, a substantial burden on their caregivers and high costs to payors. Data from our North American pivotal study demonstrate the potential for **alfa**pump to transform the lives of these patients by virtually eliminating the need for paracentesis and delivering clinicially important improvements in quality of life. We anticipate FDA approval in the second half of 2024 and look forward to introducing the **alfa**pump through our own specialy salesforce focused on US liver transplant centers."*

The PMA filing is based on the successful execution of Sequana Medical's pivotal POSEIDON study, a landmark study across 18 centers in the US and Canada with a total of 69 patients implanted with the **alfa**pump. The primary effectiveness endpoints at six months post-implantation in the Pivotal Cohort[i] exceeded the predefined thresholds with statistical significance, and primary safety endpoint data was in line with expectations[ii]. Data at 12 months post-implantation continued to show a strong and durable clinical profile, virtually eliminating

the need for therapeutic paracentesis and delivering a clinically meaningful improvement in patients' quality of life[iii].

Data from the patient preference study and a matched cohort analysis of the NACSELD[iv] registry with the POSEIDON Pivotal Cohort indicated that US patients have a strong preference for the **alfa**pump vs standard paracentesis procedures and that the safety profile of the **alfa**pump is comparable to standard of care.

The North American market of recurrent and refractory ascites due to liver cirrhosis is forecast to grow 6-7% per year, from 78,000 patients in 2025, reaching a market opportunity for **alfa**pump of over $2.5 billion by 2035, with NASH being the major driver of growth[v]. To date, over 1,000 **alfa**pump systems have been implanted.

For more information, please contact:

Sequana Medical

Lies Vanneste
Director Investor Relations
E: IR@sequanamedical.com
T: +32 (0)498 053579

Strong and durable clinical alfapump profile demonstrated in pivotal POSEIDON study

Pivotal Cohort patients from the POSEIDON study had a 100% median reduction in therapeutic paracentesis in the 4-6 month post-implant period vs the three month pre-implant period, and this was maintained in the 7-12 month post-implant period. These data show that the **alfa**pump has a sustained effect on controlling ascites, virtually eliminating the need for therapeutic paracentesis.

During the 0-6 month post-implant period, the **alfa**pump was explanted in six Pivotal Cohort patients (three due to wound or skin erosion and three due to patient-reported discomfort of moderate severity) and in two Pivotal Cohort patients during the 7-12 month post-implant period (one due to a urinary tract infection and one due to wound dehiscence). The number of Major Adverse Events (MAEs[vi]) and serious infections were in line with expectations. Importantly, creatine and eGFR[vii] levels of **alfa**pump-treated patients over 12-month follow-up indicated a stable renal function. Overall, these safety data indicate that the **alfa**pump has a robust safety profile over long-term follow-up. In addition, a matched cohort analysis of the NACSELD registry with the POSEIDON Pivotal Cohort indicated that the safety profile of the **alfa**pump is in line with expectations and comparable to standard paracentesis procedures.

Patients from the POSEIDON study had a clinically meaningful improvement in quality of life (assessed through the physical component score of SF36, a general health quality of life measure, and the Ascites Q score, a quality of life measure specific for patients with ascites) at 6 months post-implant vs three months pre-implant and maintained this at 12 months post-implant, despite disease progression.

The overall trend in survival[viii] in patients implanted with the **alfa**pump in the POSEIDON study remained positive over a longer term, with a Kaplan-Meier estimate indicating over 70% survival probability at 12 and 18 months post-implant. This compares favourably with the published literature reporting a predicted survival probability for refractory ascites patients with a similar MELD[ix] score and receiving paracentesis of approximately 17% at 12 months and 5% at 18 months[x].

Data from the POSEIDON study will be submitted for publication in a peer-reviewed journal.

Outcome patient preference study[xi]

The patient preference study was conducted by RTI Health Solutions using a discrete-choice experiment methodology to elicit patient preference for attributes of an implantable pump as a novel interventional treatment for ascites. In total, 125 US patients with a comparable patient profile as the Pivotal Cohort in the POSEIDON study, completed the survey. Results indicate that US patients have a strong preference for the **alfa**pump vs standard paracentesis procedures, with reduction in paracentesis frequency and additional ascites good health days as important attributes. The study also indicated that the **alfa**pump benefit-risk profile from the POSEIDON Pivotal Cohort is superior to what patients require from a novel implantable pump.

About recurrent and refractory ascites due to liver cirrhosis

Recurrent and refractory ascites is a key complication of liver cirrhosis, characterized by the accumulation of fluid in the abdomen. These patients can have up to 15 liters of extra fluid in their bodies, causing many health issues and severely impacting their daily life. Although diuretics are standard of care, the problem is that in many patients they are no longer effective and / or tolerable, requiring patients to undergo regular paracentesis. Paracentesis is a painful and burdensome procedure that drains ascites from the abdomen using a large needle over an extended period, with only short term benefit for the patients, requiring frequent hospitalizations and severely impacting their quality of life.

The North American market for recurrent or refractory ascites due to liver cirrhosis is estimated at 78,000 patients in 2025, and this number is expected to grow at 6-7% per year, reaching over 170,000 patients in 2035 due to the strong growth of non-alcoholic steatohepatitis (NASH) / metabolic dysfunction-associated steatohepatitis (MASH).

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 to the US FDA in December 2023 having reported positive primary and secondary endpoint data from the North American pivotal POSEIDON study of the **alfa**pump 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 and the randomized cohort of up to a further 30 patients will start following DSMB approval, planned for Q1 2024.

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] The Pivotal Cohort is used for the primary effectiveness endpoints and consists of 40 patients implanted with the **alfa**pump
[ii] Data reported in press release of 25 October 2022
[iii] Data reported in press release of 19 October 2023
[iv] NACSELD is the North American Consortium for the Study of End Stage Liver Disease. A matched cohort analysis was conducted by an independent group comparing outcomes of decompensated cirrhosis patients from the NACSELD-III registry to those from the POSEIDON study; see press release of 19 October 2023
[v] Based on US and Canada market assessment conducted by highly experienced international consulting group, estimating over 170,000 patients with recurrent or refractory ascites in North America by 2035, with estimated incidence of 60% and based on $25K for price of **alfa**pump
[vi] MAEs were pre-defined in the protocol together with the principal investigators and FDA as one of the following events: AKI > stage 2, hepatorenal syndrome, hepatic encephalopathy > grade 2, spontaneous bacterial peritonitis and reccurent or refractory infection related to paracentesis or the **alfa**pump system, procedure or therapy
[vii] eGFR: estimated Glomerular Filtration Rate, a measure of kidney function
[viii] POSEIDON study not powered for survival
[ix] MELD: Model for End-Stage Liver Disease scoring system based on laboratory parameters, and is used to predict three-month survival rate and consider patients for liver transplantation
[x] Salerno et al., Gastroenterology 2007; 133:825-834; figure 2: estimated probability of death according to treatment allocation (TIPS or paracentesis) in hypothetical patients with different MELD scores
[xi] Data reported in press release of 19 October 2023