EDISON

Sequana Medical

Pipeline update

DSR 2.0 moving forward

Pharma and biotech

Following sustained positive effects from the SAHARA I study in restoring diuretic response (DR) in heart failure (HF) patients with persistent congestion, Sequana will focus on advancing its Direct Sodium Removal (DSR) programme using its second-generation product (DSR 2.0) as applied through a peritoneal catheter ('short-term DSR'). This should provide a more straightforward regulatory pathway than the alfapump DSR combination approach studied previously. The company continues to expect to report top-line data for its North American POSEIDON study of alfapump in recurrent and refractory ascites (RRA) in Q422 and it plans to submit a US premarket approval (PMA) application in H223. We have reassessed the potential market opportunity for DSR 2.0, and revised our clinical development timeline assumptions, pushing back our potential DSR launch forecast from H226 to 2028. We now derive an equity valuation per basic share of €12.38 for Sequana Medical, versus €13.12 previously.

Year end	Revenue (€m)	PBT* (€m)	EPS* (€)	DPS (€)	P/E (x)	Yield (%)
12/20	1.0	(19.0)	(1.25)	0.0	N/A	N/A
12/21	0.4	(24.4)	(1.36)	0.0	N/A	N/A
12/22e	0.6	(23.3)	(0.98)	0.0	N/A	N/A
12/23e	0.7	(24.2)	(1.01)	0.0	N/A	N/A

Note: *PBT and EPS are normalised, excluding amortisation of acquired intangibles, exceptional items and share-based payments.

SAHARA I shows lasting improvements in DR

Intensive DSR therapy was shown in SAHARA I to help eliminate persistent congestion and restore DR in previously diuretic-resistant HF patients. The most material takeaway from the trial, in our view, is that the need for loop diuretics medication was significantly lowered for an extended period (lasting up to 11 months following completion of the intensive DSR therapy round).

MOJAVE US study on DSR 2.0 to start in Q123

DSR 2.0, based on icodextrin and dextrose, is expected to have an improved therapeutic and more favourable safety profile compared to first-generation product (DSR 1.0) studied in SAHARA and RED DESERT, as it is designed to provide a longer dwelling time with slower sodium removal. Sequana plans to expand SAHARA to include a cohort (of up to five patients) who will use DSR 2.0, with results expected in Q422. The data are expected to support Sequana's US IND filing for MOJAVE, a Phase Ib/IIa US trial assessing DSR 2.0 as short-term DSR therapy in chronic HF patients with persistent congestion. MOJAVE study recruitment is planned to start in Q123, with top-line data anticipated in H124.

Valuation: Adjusting pipeline rNPV to €276m

Following adjustments to our DSR 2.0 assumptions, and after rolling forward our estimates and our forex assumptions ($1.02/€ vs $1.09/€ previously), we now obtain a pipeline rNPV valuation of €276.4m versus €287.8m, previously. After adding H122e net cash of €17.6m (excluding lease liabilities), we obtain an equity valuation of €294.1m or €12.38 per share (€11.11 fully diluted), versus €13.12 previously (€12.19 fully diluted).

15 August 2022

Price	**€6.20**
Market cap	**€134m**
	$1.02/€
Net cash (€m) at 31 December 2021 (excluding €0.8m lease liabilities)	2.3
Shares in issue	23.75m
Free float	45%
Code	SEQUA
Primary exchange	Euronext
Secondary exchange	N/A

Share price performance

%	1m	3m	12m
Abs	17.9	9.6	(18.2)
Rel (local)	14.7	12.1	(7.5)
52-week high/low		€8.38	€4.86

Business description

Based in Belgium, Sequana Medical develops products to treat diuretic-resistant fluid overload, a frequent complication of liver disease and heart failure. Its proprietary alfapump and DSR approaches aim to provide significant clinical and quality-of-life benefits in these fluid overload conditions.

Next events

IND filing for MOJAVE Phase Ib/IIa DSR 2.0 study	Q422
POSEIDON alfapump pivotal study primary efficacy data	Q422

Analyst

Pooya Hemami OD MBA CFA +1 646 653 7026

healthcare@edisongroup.com

Edison profile page

Sequana Medical is a research client of Edison Investment Research Limited

Investment summary

Company description: Innovative solutions for fluid overload

Sequana Medical is a commercial-stage medical device company based in Belgium that first listed in 2019 on the Euronext exchange. Near-term commercial prospects are driven by its proprietary alfapump platform for the treatment of RRA related to liver disease and malignant ascites (ie ascites resulting from cancer). As discussed in our initiation report, ascites is a painful and potentially debilitating complication of such diseases and while diuretic drugs are the standard of care (SoC), resistance often develops and remaining alternative treatment options present risks and/or significant patient burden. The fully implanted, wirelessly charged alfapump automatically pumps fluid from the abdomen into the bladder and is positioned as a convenient and effective chronic treatment. The alfapump is undergoing a pivotal US registration study, POSEIDON, with primary endpoint data expected in Q422 (potential US launch in mid-2024). It is also CE marked and commercialised in parts of Europe for this indication. Sequana's larger opportunity lies within its DSR programme for chronic HF patients with persistent congestion. Following encouraging data including sustained improvements in DR from its Phase IIa SAHARA DSR study in patients with persistent congestion despite maximal loop diuretic therapy, the company plans to start the MOJAVE US Phase Ib/IIa study in early 2023 in a similar patient population, using its second-generation product (DSR 2.0).

Valuation: Pipeline rNPV of €276m reflects upside potential

Our Sequana valuation applies a risk-adjusted NPV model primarily valuing the North American prospects for alfapump (55% probability of success) and the EU and North American prospects for DSR 2.0 (25% probability of success, given the earlier development stage), both using a 12.5% discount rate. Following adjustments to our DSR 2.0 assumptions, and after rolling forward our estimates and forex assumptions ($1.02/€ vs $1.09/€ previously), we now obtain a pipeline rNPV valuation of €276.4m versus €287.8m, previously. After adding H122e net cash of €17.6m (excluding lease liabilities), we obtain an equity valuation of €294.1m or €12.38 per share (€11.11 fully diluted), versus €13.12 previously (€12.19 fully diluted).

Financials: Funded into Q323 with recent Kreos debt facility

As the company is no longer advancing an alfapump DSR combination product, we have reduced our total R&D expense forecasts for the DSR programme, and this is offset by increased R&D cost projections for the alfapump RRA programme. We expect a net FY22e operating cash burn rate of €23.4m, and now expect a net operating burn rate of €23.4m in FY23e (vs €22.0m previously) and €24.8m in FY24e (vs €28.0m, previously). We estimate H122e net cash of €17.6m and now assume future total financing expectations of €110m (vs €100m previously), which we model that Sequana will raise over the next few years until it starts to generate sustained positive operating cash flows (which we now expect in H128 vs H127 previously given that we now expect DSR commercialisation in 2028 vs H226 previously). As per usual Edison policy, these fund-raising requirements are modelled as illustrative debt. The company in July entered into a €10m debt financing facility with Kreos Capital, which we assume will fulfil part of our expected funding requirements. The company expects that the facility, if fully utilised, would extend its cash runway into Q323 (vs its prior guidance of Q223).

Sensitivities: Development, partnership, financing risks

In addition to the usual regulatory and development risks, Sequana will need to demonstrate clear benefits of the alfapump over alternate ascites treatments and effectively promote the product to the medical community and hepatologists to optimise penetration. The company must also develop

its own US salesforce and it has no existing experience in this region. While alfapump uptake in Europe has been slow, North American prospects could be stronger given the rising prevalence of non-alcoholic steatohepatitis (NASH). For DSR, Sequana will depend on the commercialisation efforts and capabilities of a potential sales and distribution partner, as well as on securing a transaction at satisfactory terms and in a timely manner. Sequana will also need to have access to further capital to advance its programmes, and if its expenditures are higher than forecast and/or if revenue is below our expectations, its capital needs may be higher than we project. While our model accounts for the financing(s) as long-term debt, the company may need to issue equity instead, at pricing that may not be favourable for current shareholders and could lead to significant dilution. Finally, the success of Sequana's products may depend on its ability to defend the IP assets surrounding them.

SAHARA data pave way for DSR 2.0

Following completion of enrolment from Part I of its Phase IIa SAHARA DSR study in patients with persistent congestion despite maximal loop diuretic therapy and positive sustained data discussed further below, Sequana has refined its DSR development strategy. The company will focus on applying DSR therapy using its second-generation product (DSR 2.0) as applied through a peritoneal catheter ('short-term DSR'), rather than the alfapump DSR drug/device combination (see our initiation report for further details) therapy previously studied in the SAHARA and RED DESERT trials. Effectively, given indications of robust treatment persistence (a reduced need for diuretics medication) for up to 11 months shown in SAHARA, Sequana believes that a focused three- to four-week session of DSR therapy using a peritoneal catheter ('short-term DSR') could be sufficient to provide six to 12 months of therapeutic effect. As alfapump implantation may not be needed to reach a sustained treatment effect, Sequana believes the short-term DSR approach can reliably deliver the desired therapeutic effect (improving cardio-renal parameters and reducing reliance on loop diuretics over a prolonged duration).

Furthermore, the regulatory approval pathway for short-term DSR therapy with DSR 2.0 is likely to be more straightforward than the alfapump device/DSR therapy ('alfapump DSR') combination studied in SAHARA and RED DESERT, since DSR 2.0 would be regulated as a drug by the FDA, whereas the alfapump DSR combination would likely have needed to be regulated as a drug-device combination. Finally, this strategy should result in cost savings compared to the company's prior parallel approach for advancing both short-term DSR and alfapump DSR in HF, as the company's prior plan to start the SONORAN alfapump DSR study in H223 (which we estimate would have cost c €8m) has been discontinued.

SAHARA I DSR study results

As explained in our initiation report, HF can often lead to sodium retention and resulting fluid retention and accumulation (congestion). Congestion in HF patients is generally treated with diuretics in the first line, most commonly loop diuretics (eg furosemide, bumetanide and torsemide), but these drugs become less effective with disease progression. It has been estimated that more than one million US hospitalisations for HF[1] occur each year, and that c 90%[2] of these are due to fluid overload (or congestion), and about 25% of these cases due to congestion are re-admitted within 30 days (and that c 50% are re-admitted within six months).

[1] Jackson SL, Tong X, King RJ et al. Circ Heart Fail. 2018 Dec;11(12):e004873. doi: 10.1161/CIRCHEARTFAILURE.117.004873. PMID: 3056209.

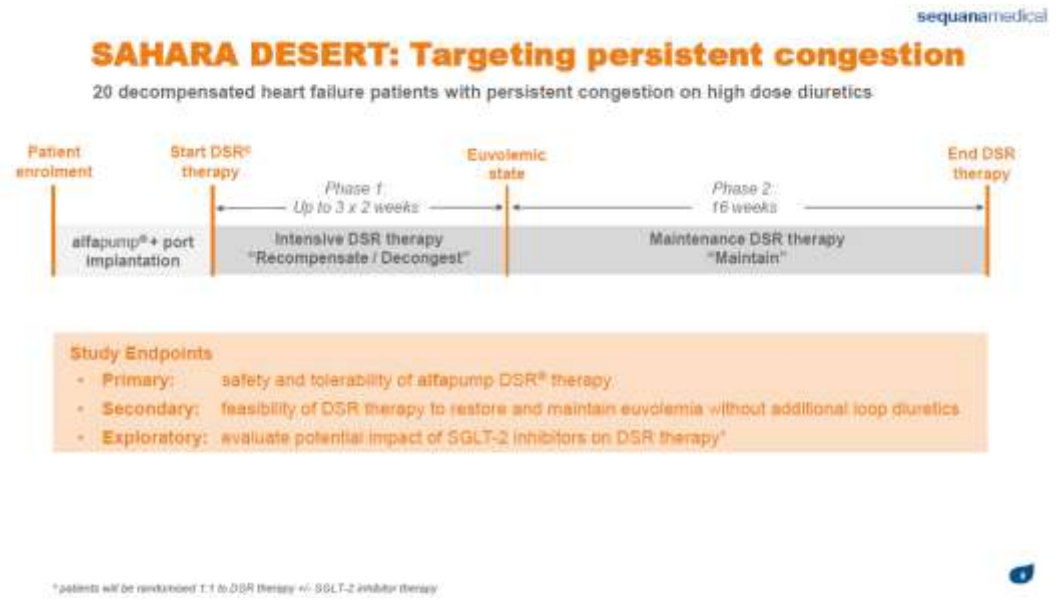
[2] Costanzo MR, Ronco C, Abraham WT et al. J Am Coll Cardiol. 2017 May 16; 69(19): 2428–2445. doi: 10.1016/j.jacc.2017.03.528.

Sequana's DSR approach aims to resolve persistent congestion through the controlled introduction of a zero-sodium therapeutic solution, which is designed to remove excess sodium in patients and then restore DR and the kidney's capacity to excrete excess fluids. While patients in the prior RED DESERT study were able to manage their fluid overload with high-dose loop diuretics, the SAHARA trial, which began enrolment in June 2021, assesses alfapump DSR in the more severely diseased HF population of patients with persistent congestion who were resistant to diuretic medication at study onset.

Our December 2021 note on interim SAHARA data described this trial's protocol in greater detail, but in summary, at study onset, subjects are implanted with the alfapump device and discontinue all loop diuretics and then undergo DSR therapy (facilitated by the alfapump implant) in two phases: an intensive treatment phase (Phase I), followed by maintenance treatment and follow-up phase (Phase II) of 16 weeks. Phase I lasts between two and six weeks (depending on patient response) where patients receive up to once daily titrated DSR treatments delivered through an implanted port (port-a-cath) into the peritoneal cavity. During Phase II, subjects will receive DSR therapy in a monthly maintenance treatment session for four months in total.

All patients underwent a 'diuretic challenge' with an IV administration of 40mg furosemide, prior to commencing DSR dosing, and again after Phase I, to measure their diuretic responsiveness and six-hour sodium excretion (ie as measured in urine output) at both study time points.

Exhibit 1: SAHARA trial protocol

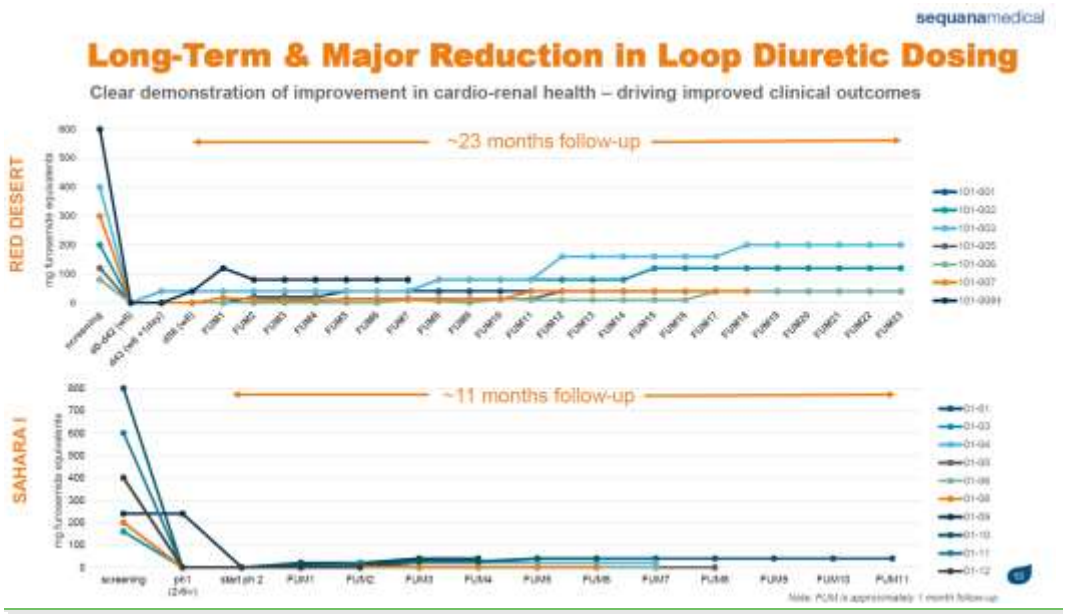


Source: Sequana Medical presentation

In the updated data released in July 2022, results were reported on 10 evaluable patients after an intensive round of DSR therapy using the alfapump DSR system and the first-generation zero-sodium DSR infusate solution (DSR 1.0), which consists of a 10% dextrose sugar solution.

DR was markedly improved in all 10 evaluable patients compared to baseline, showing a more than doubling of sodium excretion levels (towards near-normal levels, although specific figures were not provided). All evaluable SAHARA I patients enrolled in the original cohort design met proof of concept, with a >30% mean reduction of NT-proBNP vs baseline (indicating improved cardio-renal status) and stable renal function (no significant change in eGFR vs baseline). Patients also showed a mean 6kg weight loss vs baseline (restoration of normal bodily fluid volume), and a significant reduction in their required loop diuretic dosing (nine out of 10 had a reduction of more than 90%), as shown in Exhibit 2 (bottom diagram shows the SAHARA I cohort data).

Exhibit 2: Reduction in DSR dosing in RED DESERT and SAHARA I studies



Source: Sequana Medical

Altogether intensive DSR therapy was shown in SAHARA I to help eliminate persistent congestion and restore euvolemia (ie normal bodily fluid volume) and DR in previously diuretic-resistant HF patients. The most material takeaway from the trial, in our view, is that the need for loop diuretics medication was significantly lowered for an extended period (lasting up to 11 months following completion of the Phase I intensive DSR therapy round), as shown below.

Exhibit 3: Sustained reduction in diuretics dosing among 10 evaluable SAHARA I patients

Evaluable patient	Number of 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%

Source: Sequana Medical

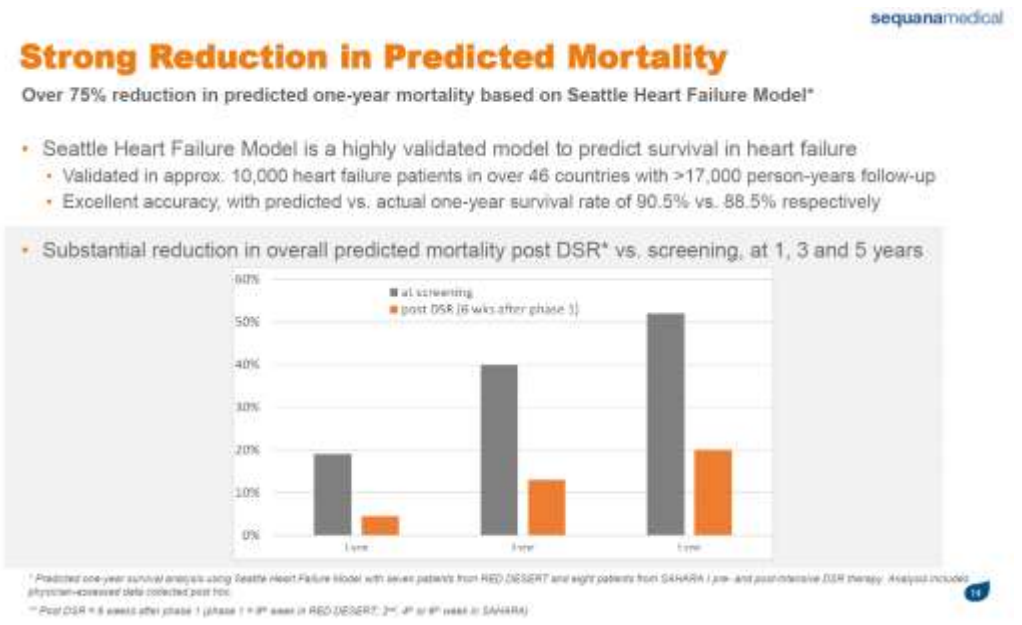
This sustained reduction in diuretics dosing (for up to 11 months) underpins the company's shift in strategy to focus the DSR programme on short-term DSR therapy, as the alfapump implantation (which would facilitate regular DSR dosing) does not appear to be required to ensure a prolonged treatment effect. Sequana believes that based on RED DESERT and SAHARA I data to date, an intensive treatment period of three to four weeks of DSR therapy in a controlled setting (ie a physician's office) using a peritoneal catheter could be sufficient to provide for six to 12 months of important clinical benefits, and would not require permanent device implantation.

Reduced hospitalisations, lower predicted death rates

Patients treated with DSR therapy in both RED DESERT and SAHARA did not experience any congestion-related HF hospital re-admissions during their follow-up period (16 weeks in the case of SAHARA). This compares with a c 25% predicted 30-day re-admission rate (Costanzo MR et al. 2017, cited above) in HF patients admitted to hospital for persistent congestion. Although we note that these are not identical populations in terms of disease severity, as HF patients with persistent

congestion admitted into the SAHARA study may differ in disease status from those HF patients admitted to hospital for their persistent congestion, we believe that the lack of congestion-related hospital admissions during the follow-up period is highly encouraging. Based on the Seattle Heart Failure Model, the company has conducted analysis using post-hoc data that predicts that, based on physician-collected data (including congestion status, cardio-renal parameters, etc) at six weeks past Phase I of SAHARA I and RED DESERT studies, subjects having completed the DSR therapy would have a c 75% lower predicted one-year mortality post-DSR therapy (c 5%) versus at screening (c 20%). This type of data, if expanded upon in future trials, can be very compelling in an eventual regulatory filing and/or for providing support for the commercial roll-out if the product is approved.

Exhibit 4: Predicted mortality analysis based on SAHARA I data



Source: Sequana Medical

Effectively, the SAHARA results to date show that following DSR therapy, renal function (such as the ability to remove excess fluid) is restored for an extended period as patients can substantially reduce their dosage of diuretic medications (compared to pre-DSR intervention) for many months. The results suggest DSR can effectively and rapidly eliminate persistent congestion and restore euvolemia in diuretic-resistant HF patients, and show improvements in certain cardio-renal parameters.

DSR 2.0 product to be tested in SAHARA II, then MOJAVE study

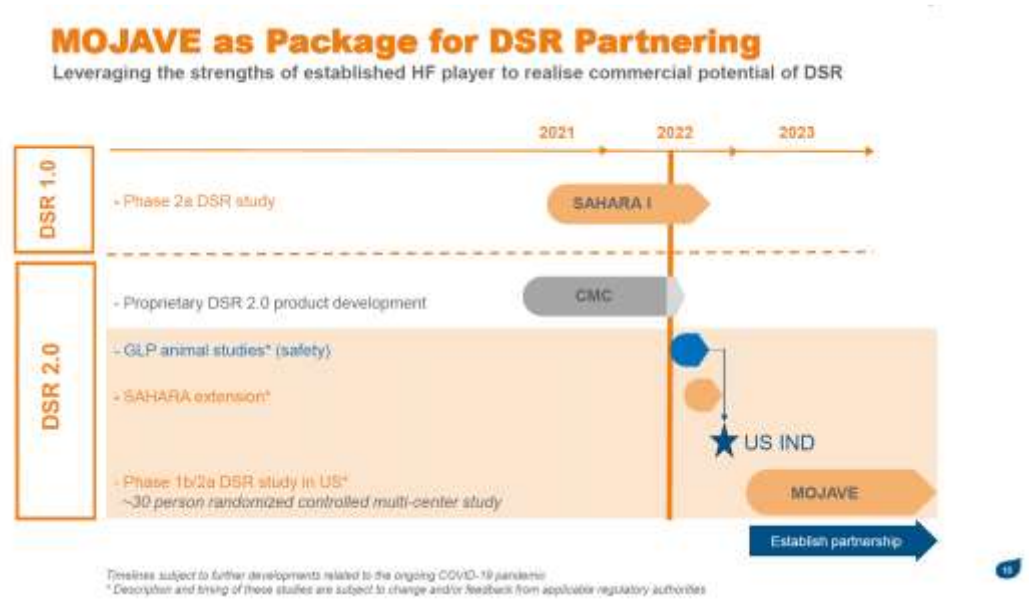
The company's next step to advance the short-term DSR programme is to assess its next-generation DSR product, DSR 2.0, in a new cohort within its SAHARA study (to be termed SAHARA II). This new cohort of up to five patients will use DSR 2.0 (instead of DSR 1.0) in combination with the alfapump system (retained to maintain consistency with other aspects of the SAHARA study), with results expected in Q422.

DSR 2.0, a proprietary formulation of icodextrin and dextrose, is expected to have an improved therapeutic and favourable safety profile compared to first-generation solution (DSR 1.0) studied in SAHARA and RED DESERT, as it is designed to provide a longer dwelling time (ie the length of time the drug product will remain in the peritoneal cavity) and slower diffusion of the excess sodium from the bloodstream to the DSR solution. The slower sodium diffusion rate (from the bloodstream to the DSR solution) is expected to reduce the risk of hyponatremia (low blood sodium), which should make the therapy easier to use. This improved profile could potentially reduce the amount of

solution that needs to be administered to render an equivalent therapeutic response (ie as the longer dwelling time could enable a larger quantity of sodium to be removed, thereby reducing the quantity of drug product required per dose). The company has been granted intellectual property for DSR 2.0 and aims to market it as a drug to be delivered through a peritoneal catheter. We believe the GLP (preclinical) work required for the DSR 2.0 programme is largely complete.

SAHARA II data are expected to support Sequana's US IND filing for MOJAVE, a Phase Ib/IIa US trial assessing DSR 2.0 as short-term DSR therapy in chronic HF patients with persistent congestion. The MOJAVE IND is expected to be filed in Q422, with recruitment planned to start in early 2023 leading to the potential release of top-line data in H124. We assume that short-term DSR patients will receive daily c 30-minute sessions of DSR 2.0 therapy (administered via a peritoneal catheter) for seven days, followed by two to three DSR 2.0 therapy sessions per week for the subsequent three weeks, and then be monitored afterwards. Interim data for MOJAVE could be released in H223 and if positive, could potentially support partnership or out-licensing opportunities.

Exhibit 5: DSR 2.0 development strategy and timelines



Source: Sequana Medical

The company may consider partnership/out-licensing opportunities for DSR 2.0 once interim MOJAVE data are available. We assume the company and/or its potential partner will start a confirmatory Phase IIb study in H224, following the conclusion of MOJAVE, which could then lead to the start of Phase III registration enabling trials in H225 (if two registration studies are required, we expect them to be run in parallel). This could potentially lead to launch in 2028 (versus our prior estimate of an H226 potential launch). We have pushed back our DSR 2.0 launch timing estimates to reflect the company's updated guidance for the start and completion of MOJAVE, and we are also slightly extending our duration estimates for the Phase III registration studies and for the timing between regulatory New Drug Applications (NDAs) and potential market approvals.

Exhibit 6: DSR 2.0 for congestion in heart failure milestones and timelines

Event	Start date	Approximate completion
SAHARA II feasibility study in decompensated HF patients with DSR 2.0	Q322	Q422
MOJAVE Phase Ib/IIa short-term DSR US study	Q123	H124
Phase IIb study for short-term DSR	H224 (*)	H225 (*)
Registration-enabling Phase III short-term DSR trials	H225 (*)	H127 (*)
Partnership negotiations for alfapump DSR and short-term DSR	Mid-2023 (*)	Mid-2025 (*)
Potential launch in US, Europe and Canada	2028 (*)	

Source: Company guidance. Note: *Edison Investment Research assumptions.

Alfapump for ascites, an area of rising medical need

Sequana's more near-term commercial opportunity lies in its proprietary alfapump device being advanced for RRA. The alfapump received CE mark clearance in 2011 and is commercialised in Germany and France. A study to support reimbursement is also underway in France, and all current sales from France come from this study. Sequana receives revenues for the alfapump implants used in the study, which itself is sponsored by the French government. The company remains on track to report primary efficacy data from the POSEIDON alfapump North American pivotal study in Q422, and it expects to file a US premarket application for alfapump in RRA in H223, a slight delay to its prior estimate of mid-2023 given that the biocompatibility testing required to support the application has been extended by c three months. We continue to anticipate that the product could be launched in the US and Canada in mid-2024.

Ascites is the accumulation of protein-containing fluid within the abdomen, a complication of late-stage liver disease and associated with poor prognosis. The condition results in loss of appetite, shortness of breath, mobility and sleeping difficulties, and can predispose patients to develop bacterial peritonitis.[3] Ascites is predominantly caused by high blood pressure in the hepatic portal veins (portal hypertension), often due to liver cirrhosis (scarring). Cirrhosis is often caused by alcohol, hepatitis and increasingly by NASH. There are over 240,000 cases of ascites due to cirrhosis in the seven major markets,[4] and cirrhotic patients with ascites have mortality rates estimated at between 50% within two years[5] and around 44% within five years.[6]

Often, a low-sodium diet and diuretic medications can help eliminate the excess ascetic fluid, but in c 5–20% of ascites cases,[7, 8] DR develops where fluid accumulation persists despite medication use (or diuretic-induced complications occur), resulting in refractory ascites (RA). RA patients have a one-year survival rate of under 50%.[9] Remaining treatments for RA are repeated therapeutic paracentesis (TP), which is burdensome, costly and time-consuming, and/or transjugular intrahepatic portosystemic shunt (TIPS), which is associated with hepatic encephalopathy (HE). Ascites can also be a common complication of certain cancers (termed malignant ascites), which accounts for c 10% of ascites cases.[10]

RA patients are often candidates for liver transplant, but, given the lack of available supply and other intervention risks, the common treatment at this stage is TP, which is also referred to as large volume paracentesis (LVP) when the volume drained exceeds five litres. The duration of TP varies from 30 minutes to 24 hours, and the company estimates that medical costs for TP are around $1,500–1,800 per treatment, which can occur 2–3x per month in patients with RA. TP requires patients to stay in hospital for up to 48 hours and only provides temporary relief, as often a cycle

---

3 Gerbes AL (ed): Ascites, Hyponatremia and Hepatorenal Syndrome: Progress in Treatment. *Front Gastrointest Res*. Basel, Karger, 2011, vol 28, pp 23–31

4 DelveInsight Business Research, LLP report on Ascites Market. 13 April 2021. www.prnewswire.com/news-releases/ascites-market-projected-to-garner-healthy-growth-stoked-by-the-expected-launch-of-emerging-therapies-during-the-forecast-period-20212030-asserts-delveinsight-301267783.html

5 Mirza MS, Aithal GP. Portal hypertension and ascites. *Surgery*. 2007;25(1):28–33

6 Planas R, Montoliu S, Balleste B, et al: Natural history of patients hospitalized for management of cirrhotic ascites. *Clin Gastroenterol Hepatol* 2006;4: 1385–1394.

7 Santos J, Planas R, Pardo A, et al. *Journal of Hepatology*. 2003;39(2):187–192.

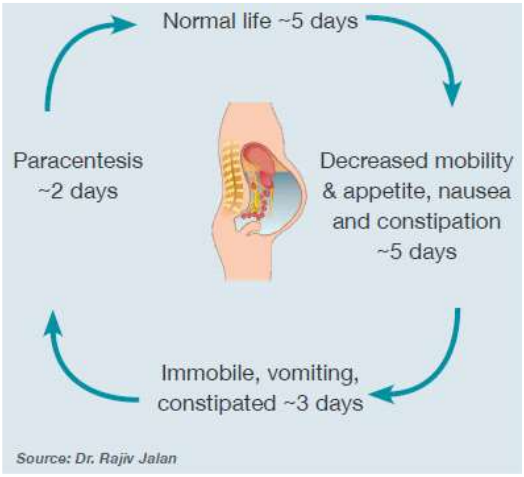
8 DelveInsight Business Research, LLP report on Ascites Market. 13 April 2021. www.prnewswire.com/news-releases/ascites-market-projected-to-garner-healthy-growth-stoked-by-the-expected-launch-of-emerging-therapies-during-the-forecast-period-20212030-asserts-delveinsight-301267783.html

9 Fede G, D'Amico G, Arvaniti V, et al. *J Hepatol*. 2012 Apr;56(4):810-8. doi: 10.1016/j.jhep.2011.10.016. Epub 2011 Dec 13. PMID: 22173162 Review.

10 Saif MW, Siddiqui IAP, Sohail MA. Ann Saudi Med. 2009 Sep-Oct; 29(5): 369–377. doi: 10.4103/0256-4947.55167 PMID: 19700895

develops where patients undergo LVP, feel much improved for up to a week but then ascites accumulates with symptoms worsening before another LVP is needed.

Exhibit 7: Paracentesis treatment cycle for RA patients



Source: Sequana Medical

The remaining FDA-approved therapeutic option for RA is TIPS, but as the procedure causes much of the patient's subsequent blood circulation to evade the liver's detoxification processes, it can often increase the risk of HE, particularly in older patients, as neurotoxins and ammonia can then accumulate in the general blood circulation. Altogether, TIPS is contraindicated in many RA patients, particularly in those over age 65, those with advanced liver disease (mostly Child-Pugh C classification), and those with HF and/or pulmonary hypertension.[11] The only curative treatment for late-stage liver disease is a transplant but availability is minimal, and patients will require lifelong immunosuppression drugs post-implantation to prevent organ rejection. In 2019, 8,906 liver transplants were performed in the United States, up 0.1% y-o-y and more than in any previous year.[12]

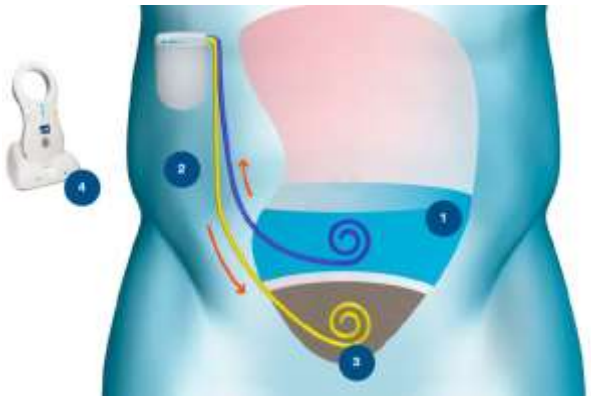
Alfapump presents a novel platform to treat liver ascites

The alfapump is designed to offer a convenient and unobstructive long-term therapy that aims to improve patient independence and quality of life (QoL), and reduce their need to frequent healthcare facilities for time-consuming and uncomfortable TP. The alfapump can pump up to four litres of ascites-containing fluid per day from the abdomen into the bladder, where it is eliminated via urination.

[11] Bellot P, Welker MW, Soriano G, et al. *J Hepatol*. 2013 May;58(5):922-7. doi: 10.1016/j.jhep.2012.12.020. Epub 2013 Jan 11.PMID: 23318604

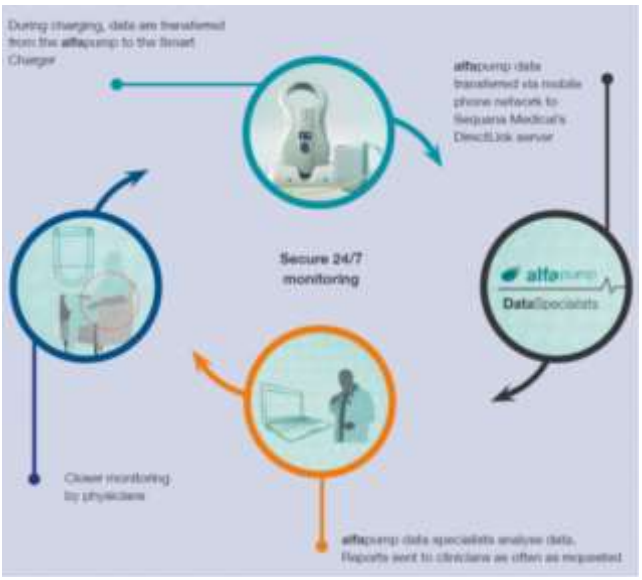
[12] US Organ Procurement and Transplantation Network 2020 Annual Report. https://srtr.transplant.hrsa.gov/annual_reports/2020/Liver.aspx

Exhibit 8: Diagram of alfapump system and placement



Source: Sequana Medical. Note: 1) Automatic and continuous removal of fluid from the abdomen; 2) fluid is pumped into bladder; 3) fluid leaves the body through normal urination; 4) wireless charging and communication for monitoring.

Exhibit 9: Alfapump charging cycle and DirectLink system



Source: Sequana Medical

Ascites growth rate influenced by increasing NASH prevalence

The US Centers for Disease Control estimates that in 2018 more than 4.5 million US adults were diagnosed with chronic liver disease.[13] While alcohol abuse and hepatitis are the most common causes of liver ascites, the emergence of non-alcoholic fatty liver disease (NAFLD) (and consequently NASH) is a more recent contributor and is attributed to lifestyle-related disorders including obesity and type 2 diabetes. NAFLD is already one of the most common causes of chronic liver disease with an estimated global prevalence approaching one billion people.[14] Between 21%[15] and 26%[16] of the US population have NAFLD. Between 20% to 30% of NAFLD patients are expected to progress to NASH within about 10 years[17] and once NASH develops, c 10% should progress to cirrhosis within c 10 years.

In 2015, there were an estimated 1.16m compensated cirrhosis cases and 134,400 decompensated cirrhosis cases in the United States.[18] Patients with decompensated cirrhosis have at least one

[13] US Centers for Disease Control. www.cdc.gov/nchs/fastats/liver-disease.htm

[14] Loomba R, et al. (2013) The Global NAFLD Epidemic. *Nat Rev Gastroenterol Hepatol* 10, 686-690.

[15] Younossi Z, et al. (2017) Global Burden of NAFLD and NASH: Trends, Predictions, Risk Factors and Prevention. *Nat Rev Gastroenterol Hepatol* 109, 1-10.

[16] Estes C, Razavi H, Loomba R, Younossi Z, Sanyal AJ. *Hepatology.* 2018 Jan;67(1):123-133. doi: 10.1002/hep.29466. Epub 2017 Dec 1.

[17] Loomba R, et al. (2019) The 20% Rule of NASH Progression: The Natural History of Advanced Fibrosis and Cirrhosis Caused by NASH. *Hepatology* 70, 1913.

[18] Estes C, Razavi H, Loomba R, Younossi Z, Sanyal AJ. *Hepatology*. 2018 Jan;67(1):123-133. doi: 10.1002/hep.29466. Epub 2017 Dec 1.

complication, very often ascites, and have a median survival time of two years.[19] Once ascites develops, between 5% and 20% of these patients will develop RA.[20, 21]

With NASH prevalence expected to grow ~60% by 2030,[22] we expect the profile of the typical ascites patient to shift from mostly alcohol- and hepatitis-related cases towards an older, NASH-driven demographic with potentially greater access to the healthcare system and/or compliance to recommended treatments. Further, largely because of the increased risk of HE, TIPS is generally less suitable for the older population demographic that NASH ascites is more likely to affect.

The POSEIDON study is the key to potential US launch

Our initiation report discusses many of the earlier alfapump studies in RRA in greater detail, but the key trial to monitor in our view is the POSEIDON North American pivotal study in patients with RRA due to liver cirrhosis. The trial started in 2019 and is designed to support alfapump approval and reimbursement in the United States and Canada. The study is a single-arm and open-label, within-subject crossover study, whereby patients will serve as their own controls. Following enrolment, patients enter a three-month pre-implant observation period in which they receive SoC therapy, consisting of TP, before the alfapump is implanted. Eligible patients will be implanted with the alfapump and during the three-month stabilisation period, their alfapump settings will be adjusted as needed and patients will be fully trained. After the stabilisation period, a three-month post-implant observation period begins. The primary effectiveness outcomes include:

- the proportion of patients with a 50% reduction in the overall average frequency of TP per month in the post-implant observation period (reflecting month four to month six after implantation) as compared to the pre-implant observation period; and
- whether at least 50% of patients receive a 50% reduction in their monthly frequency of required TP post-implantation compared to the average monthly number of TP required pre-implantation.

The primary safety endpoint is the rate of alfapump-related re-interventions as determined by the Clinical Events Committee, at six months post implantation. Albumin supplementation is also highly recommended (given that this may support renal health). Twenty-nine patients were enrolled in a training (or 'roll-in') cohort (which will be excluded from primary efficacy analysis but included in the safety analysis), to ensure centres were experienced with the alfapump before the actual pivotal (study) cohort was enrolled.

Enrolment of patients within the pivotal cohort was completed in December 2021, with the company affirming that its objective for POSEIDON was to enrol c 70 patients in the pivotal cohort, implant the alfapump in up to 50 of those patients and obtain up to 40 patients evaluable for the primary efficacy analysis. Sequana reported in April 2022 the completion of all POSEIDON alfapump implantations, with the total number of implanted patients within the pivotal cohort being 40 (out of 71 enrolled patients within that cohort). Given the severe disease status and lower life expectancy of the RRA population, we assume that a number of implanted patients may not be evaluable six months post-implantation, and hence we estimate that the number of patients evaluable for primary efficacy analysis is likely be c 30–35.

---

19 US Department of Veterans Affairs. Viral Hepatitis and Liver Disease. www.hepatitis.va.gov/cirrhosis/background/stages.asp

20 Ginès P, Cárdenas A, Arroyo V, et al. N Engl J Med. 2004 Apr 15;350(16):1646-54. doi: 10.1056/NEJMra035021. PMID: 15084697 Review.

21 DelveInsight Business Research, LLP report on Ascites Market. 13 April 2021. www.prnewswire.com/news-releases/ascites-market-projected-to-garner-healthy-growth-stoked-by-the-expected-launch-of-emerging-therapies-during-the-forecast-period-20212030-asserts-delveinsight-301267783.html

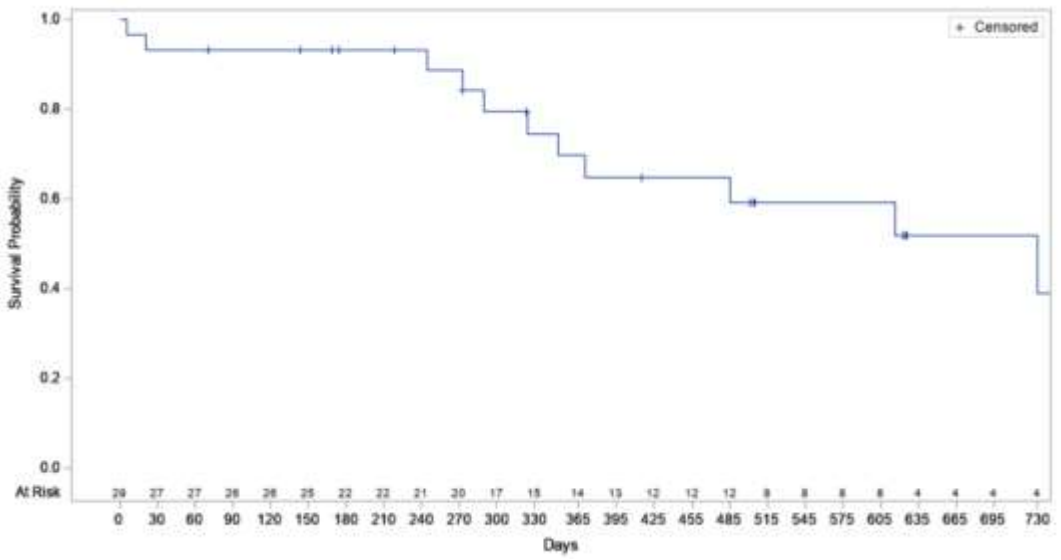
22 Estes C, Razavi H, Loomba R, Younossi Z, Sanyal AJ. *Hepatology*. 2018 Jan;67(1):123-133. doi: 10.1002/hep.29466. Epub 2017 Dec 1.

As described in a prior note, a second interim analysis of the study roll-in cohort from July 2021 showed that subjects had a greater than 90% reduction in mean frequency of TP versus baseline, and all patients experienced at least a 50% reduction in mean TP frequency per month versus baseline. As these trends substantially exceed the primary endpoints as defined in the pivotal cohort, we are confident that there is likely to be a sufficient efficacy buffer or margin (assuming the pivotal cohort data would be similar to the roll-in cohort data to date) for the pivotal cohort to still meet the primary endpoint targets despite there likely being a lower number of evaluable patients than originally planned. For instance, we estimate that a 90% reduction in the overall average frequency of TP (similar to that shown in the roll-in cohort) in a sample size of 30–35 would provide a stronger statistical signal than a 50% reduction in a sample size of 40. Further, as stated above, once enrolment in the pivotal cohort began, study centres had already accumulated more experience with the alfapump system (compared to when they were enrolling the roll-in cohort). We believe this provides the potential for the data resulting from this cohort to be more robust than that reported to date from the roll-in cohort.

Patient survival trends generally favourable in roll-in cohort

Given that the overall intent of alfapump is to improve QoL (by reducing the need for TP) in RRA patients, Sequana has not attempted to assess whether the alfapump could have any effect on overall mortality. Nonetheless, Sequana reported a preliminary interim analysis (as of 25 March 2022) of patient survival in the roll-in cohort following alfapump implantation, which showed a mean survival probability of 70% at 12 months. This compares favourably with published reports (Biggins et al as cited in the American Association for the Study of Liver Diseases Practice Guidance; Moreau et al),[23] which found a 12-month survival rate for RA patients of only c 50%.

Exhibit 10: Kaplan-Meier – preliminary survival rate analysis of roll-in cohort, 25 March 2022



Source: Sequana Medical

Given the general poor state of health of patients with RRA, including weakened immunity and poor renal function, we believe it would be challenging for any treatment to show a significant change in mortality, taking account of the multitude of conditions or events that such patients could inevitably experience and the difficulty in controlling a trial for such aspects. Hence, while we apply caution in comparing the roll-in cohort result with historical outcomes in the RRA population (given differing

[23] Biggins et al., *Hepatology*, Vol. 74, No. 2, 2021, AASLD Practice Guidance; Moreau R et al., *Liver International* 2004: 24: 457-464

study and inclusion criteria), the company's reporting of lower 12-month mortality may potentially bode well for the overall safety dossier of the device (when the PMA is to be filed in H223).

As stated above, the company continues to expect to report primary efficacy data from the POSEIDON study in Q422. We maintain our forecast that the alfapump will be launched in the United States in mid-2024. We continue to expect the opportunity for alfapump in North America to be much more robust than in Europe given the rising prevalence of NASH in this region. NASH-related cirrhosis is expected to account for a larger proportion of RRA cases in the United States and Canada, and these patients are generally older (and thus more likely to be contraindicated for TIPS), insured (those aged over 65 have government-run Medicare insurance in the United States) and well-integrated into the healthcare system.

Few competing ascites therapies under development

BioVie is developing BIV201, a continuous infusion formulation of terlipressin, a vasopressin-analogue drug approved in Europe and Australia often used to treat related complications of cirrhosis such as hepatorenal syndrome. BIV201 acts as a vasoconstrictor and is intended to reduce portal hypertension by restoring blood flow through the kidney and liver, and thereby impede the cycle of accelerating fluid generation in ascites patients. In 2019, BioVie completed a Phase IIa (n=6) trial of BIV201 in patients with RA due to advanced liver cirrhosis, where patients received the study drug via continuous infusion for up to 28 days. It reported that four of the six treated patients experienced an increase in the number of days between paracenteses between 71% and 414% compared to before initiating therapy. The company started a subsequent 30-patient Phase IIb study in 2021, where patients receive the drug via continuous infusion for two 28-day cycles. BioVie expects to report study data in early 2023, but we believe the need for prolonged continuous infusion cycles may limit the attractiveness of this treatment modality.

Noorik Biopharmaceuticals is developing a 'micro-dose' formulation of ambrisentan, an endothelin receptor antagonist approved (in the United States and Europe) for forms of pulmonary arterial hypertension. Noorik is advancing the candidate for portal hypertension and believes the lower dose of its formulation would selectively exert inhibitory action on one endothelin receptor (ETA) rather than both (ETA and ETB), and thereby provide a better therapeutic profile for this ascites-predisposing condition. Noorik had terminated a Phase II study on this portal pressure indication due to poor enrolment as a result of COVID-19 and is currently studying its ambrisentan formulation for respiratory insufficiency due to COVID-19.

DSR and alfapump forecasts

Our local-currency forecasts for alfapump in RA are generally unchanged (as reiterated in our April update note), but given the refinement in the company's DSR strategy, we have updated our assumptions for DSR 2.0.

Previously we had assumed that the company would advance both alfapump DSR and short-term DSR, with short-term DSR being positioned as a 'bridge' therapy towards alfapump DSR. With data suggesting that intensive DSR therapy (which we believe can be delivered through the peritoneal catheter, ie short-term DSR) can provide sustained effects, we now see the total HF congestion market as being treatable with the short-term DSR 2.0 platform (ie there is no more need for a separate alfapump DSR segment). Now that the alfapump device may no longer be required to deliver the desired therapeutic effects, we now assume the target potential peak market share is larger than previously, as we believe that the prior more invasive requirement for alfapump implantation served as a potential barrier for implementation. We believe physicians and patients alike will generally be more amenable to periodic treatment rounds of DSR (administered through a peritoneal catheter for around seven consecutive days at c 30-minutes per session, followed by

three weeks with less frequent dosing) once or twice yearly than the implantation of an alfapump device previously envisioned.

As a result, we assume peak US market share of 7.5% vs 4.0% previously (of an addressable market representing approximately 50% of the c 0.9m US HF patients hospitalised for fluid overload who are readmitted within six months, or reflecting c 0.45m patients per year). While the addressable market has increased, we have also lowered our net average revenue per patient estimates to reflect that the alfapump device is no longer necessary and that the DSR treatment is now being positioned as a drug rather than a drug/device combination. We now assume net US average annual revenue per patient at launch of $20,000, vs $27,500 previously. Our pricing assumption is supported by a recent meta-analysis suggesting that the median annual US hospitalisation costs for HF are $15,879 and that the DSR programme is expected to significantly reduce such costs (and potentially lead to quality-of-life benefits).

In addition, we have refined our commercial partnership assumptions. As described in our initiation report, we previously had anticipated a more complex partnership transaction whereby, with the DSR product proposed as a drug/device combination, Sequana would become responsible for all DSR-related manufacturing costs (device and drug product) and consequently we had modelled that Sequana would be entitled to a 30% transfer price on net sales. With DSR 2.0 being positioned as a drug, we believe a more conventional pharmaceutical licensing arrangement is more likely, with the licensee being responsible for all commercial (and manufacturing costs), and we now assume that Sequana would receive a royalty of 25% of net sales. We assume a license agreement will occur before mid-2025, and that the licensee/partner will fund a portion (modelled at 33%) of the pivotal US studies in the H225 to H127 time frame, which we model at €30m total cost (thus Sequana to fund c €20m). Our revised forecasts are stated below.

Exhibit 21: Sales forecasts for alfapump and DSR 2.0

	2024	2025	2026	2027	2028	2029	2030	2031
alfapump for refractory/recurrent ascites and malignant ascites								
North America (US & Canada)								
Estimated incidence of refractory and recurrent ascites	24,319	26,046	27,895	29,876	31,997	34,269	36,702	39,308
alfapump units sold	95	397	981	2,059	3,488	4,933	5,390	5,806
Effective penetration rate	0.4%	1.5%	3.5%	6.9%	10.9%	14.4%	14.7%	14.8%
alfapump product sales ($000)	2,384	10,157	26,107	56,957	100,226	147,190	167,222	187,329
Rest-of-world markets								
alfapump product sales ($000)	809	890	979	1,077	1,185	1,303	1,434	1,577
DSR 2.0 (in US, EU and Canada)								
Heart failure hospitalisations linked to volume overload (000)	2,902	2,954	3,008	3,063	3,118	3,175	3,233	3,292
Number of patients treated with DSR 2.0 (000)	-	-	-	-	8.0	19.2	41.0	69.4
DSR 2.0 net sales revenue (recognised by partner) ($000)	-	-	-	-	91,409	228,558	525,103	973,392
Net royalty revenue to Sequana Medical ($000)	-	-	-	-	22,852	57,139	131,276	243,348

Source: Edison Investment Research

Financials

As the alfapump DSR combination is no longer being advanced, we have removed the need for the previously planned SONORAN study, which we estimate would have cost €8m, thus reducing our total R&D expense forecasts for the DSR programme until its commercialisation. This effect is somewhat offset by the raising of our alfapump R&D costs in RRA by €3m (expected to be borne in FY23) to reflect the added biocompatibility studies required. The combination of both changes leads to an increase in our FY23e R&D cost and operating cash burn assumptions and a decrease in our

FY24e cost expectations. Our new FY23e and FY24e R&D expense assumptions are €14.9m and €9.3m, respectively, versus €13.5m and €13.0m, previously. We expect FY24 R&D costs to decrease y-o-y following the conclusion of the POSEIDON study in FY22 (and we model that a portion of the Phase III DSR studies will be paid by a future partner/licensee).

We continue to expect a net operating cash burn rate of €23.4m in FY22e, and now expect a net operating burn rate of €23.4m in FY23e (vs €22.0m previously) and €24.8m in FY24e (vs €28.0m, previously). In March, Sequana raised €28.4m (gross) though the issue of 5.167m shares at €5.50 per share. Given FY21 net debt of €2.28m (excluding lease liabilities), we estimate H122e net cash of €17.6m.

We have raised our future total financing expectations to €110m (from €100m previously), which we model that Sequana will raise over the next few years until it starts to generate sustained positive operating cash flows (which we now expect in H128 vs H127, previously). The increase in total funding need and revised positive operating cash flow timeline assumption is due to the pushing back of our DSR commercialisation timeline to 2028 (from H226, previously). As per usual Edison policy, we model future fund-raising requirements as illustrative debt. The company in July 2022 entered into a €10m debt financing facility with Kreos Capital, which we assume will fulfil part of our expected funding requirements. The Kreos loan facility agreement allows Sequana to request loans of up to €10m (accruing at 9.75% pa interest) in €1.5m increments on an uncommitted basis, until 30 September 2022, and the facility matures on 30 September 2025. The company expects that the facility, if fully utilised, would extend its cash runway into Q323 (vs its prior guidance of Q223). The loans do not contain covenants but are secured on the company's bank accounts, receivables and certain assets, including IP rights. Kreos also receives a €0.125m up-front transaction fee, and share purchase subscription rights for c 0.122m shares exercisable at €5.31 per right.

Valuation

We value Sequana Medical using a risk-adjusted NPV model with a 12.5% cost of capital for alfapump in North America and the DSR 2.0 programme, and a 10% rate for alfapump in ex-North American markets (where it is commercialised).

Exhibit 12: Sequana Medical rNPV assumptions

Product contribution	Indication	Stage	NPV (€m)	Probability of success	rNPV (€m)	rNPV/ basic share (€)	Launch year	Sales (€m) in 2032
alfapump in North America (net of R&D and SG&A costs)	Refractory and recurrent ascites and malignant ascites	Pivotal studying ongoing	272.3	55%	146.5	6.17	Mid-2024	204.9
alfapump in Europe and ex-NA regions (net of SG&A costs)	Refractory and recurrent ascites and malignant ascites	Commercial/ marketed	(2.3)	100%	(2.3)	(0.10)	2013	1.7
DSR 2.0 (short-term DSR)	Fluid overload in heart failure	Human feasibility studies	798.0	25%	189.5	7.98	2028	374.4*
Corporate costs			(57.3)	100%	(57.3)	(2.41)		
Total			1,010.7		276.4	11.64		
Net cash (H122e) excluding lease liabilities			17.6		17.6	0.74		
Total equity value			1,028.3		294.1	12.38		
Basic shares outstanding (000) (30 June 2022)			23,747					
Outstanding warrants and share options			2,722					
FD shares outstanding (000)			26,468					

Source: Edison Investment Research. Note: *Reflects estimate of projected royalty revenue to Sequana Medical rather than end-market commercial sales.

Following the adjustments described above, particularly with respect to the DSR 2.0 programme, and after rolling forward our estimates and our forex assumptions ($1.02/€ vs $1.09/€ previously), we now obtain a pipeline rNPV valuation of €276.4m versus €287.8m, previously. After adding H122e net cash of €17.6m (excluding lease liabilities), we obtain an equity valuation of €294.1m or €12.38 per share (€11.11 fully diluted), versus €13.12 previously (€12.19 fully diluted).

Sensitivities

Development and regulatory risk: for alfapump in RRA, if the rate of safety events in the POSEIDON study, particularly the incidence of acute kidney injury or blockage, is higher than in the MOSAIC US feasibility study, and/or if TP rates post-implantation are not sufficiently reduced, it could dampen the likelihood of approval in North America. These risks are somewhat alleviated by data reported to date from the 'roll-in cohort' component of this study, which has shown a more than 90% reduction in the mean frequency of TP versus baseline, and an acceptable safety profile, in our view. The DSR 2.0 programme has further studies and development before reaching the approvability stage, so as such it carries higher risks, but the RED DESERT and SAHARA results show proof-of-concept in terms of demonstrating a sustained lower need for diuretics and improvements in cardio-renal parameters.

Commercial and competition risk: if approved in RRA, alfapump would show a clear advantage over TP in an area of unmet medical need, but the company will need to effectively promote the product to hepatologists, interventional radiologists and the medical community at large to optimise penetration. The relatively limited traction to date in Europe could highlight possible challenges for North American adoption, but the rising prevalence of NASH as a cause of RRA and the potential for improved healthcare access compared to 'traditional' RRA causes could portend a much stronger penetration rate in this region. The company must also develop its own US salesforce and it has no existing commercial experience in this territory, although its intended strategy to target dedicated liver transplant centres appears sound. Further, while alfapump is the most advanced-stage RRA treatment candidate to our knowledge and the only one in US registration enabling trials, in the event that BIV201, ambrisentan or another future competing product obtains approval, alfapump would need to compete with these alternatives and product positioning and its relative strengths in safety and efficacy versus emerging competitors will be key in sustaining a strong market position.

Partnership risk: Sequana will be dependent on the commercialisation efforts and capabilities of its potential partner for its DSR 2.0 programme. If Sequana is unable to secure a favourable licensing deal in a timely manner, it could weaken the eventual economics Sequana could be entitled to for these programmes and/or result in additional delays before the attainment of commercial revenues.

Financing risk: we expect Sequana will need to raise additional capital before commercialising alfapump in North America and further capital to build the required salesforce needed to reach profitability in H128. We forecast €110m in financings between H222 and 2027. Difficulties or challenges in obtaining funds could affect the timing or progression of Sequana's programmes. If Sequana's expenditures are higher than forecast and/or if revenue is below our expectations, it may need to raise further capital. While our model accounts for the financing(s) as long-term debt, the company may need to issue equity instead, at pricing that may not be favourable for current shareholders and could lead to significant dilution.

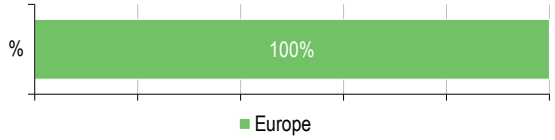
Intellectual property risk: the success of Sequana's programmes will depend on its ability to defend the IP assets surrounding them.

Reimbursement risk: to obtain optimal revenue and product penetration, Sequana and/or its partner will need to negotiate with the Centers for Medicare & Medicaid Services (CMS; likely the dominant insurer involved with payment for alfapump and DSR 2.0) and obtain favourable reimbursement terms, which we believe would also have a trickle-down effect on the terms offered by other private insurers. The FDA Breakthrough Therapy status accorded to alfapump provides some assurance of provisional CMS reimbursement for up to four years post-approval, but securing longer-term reimbursement may depend on the accumulation of post-approval efficacy data in the US Medicare population.

Exhibit 13: Financial summary

€(000)	2018	2019	2020	2021	2022e	2023e	2024e
Year-end 31 December	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS	IFRS
PROFIT & LOSS							
Revenue	1,029	971	963	371	600	690	3,131
Cost of Sales	(158)	(198)	(202)	(77)	(120)	(138)	(626)
Gross Profit	871	773	761	294	480	552	2,505
General & Administrative	(8,206)	(7,102)	(6,738)	(7,177)	(6,956)	(8,461)	(14,512)
Net Research & Development	(5,816)	(7,652)	(11,835)	(16,935)	(16,500)	(14,900)	(9,300)
Operating profit before exceptionals	(13,150)	(13,981)	(17,813)	(23,818)	(22,976)	(22,809)	(21,307)
EBITDA	(13,070)	(13,737)	(17,506)	(23,409)	(22,539)	(22,433)	(20,961)
Depreciation & other	(81)	(244)	(307)	(409)	(437)	(376)	(347)
Operating Profit (before amort. and except.)	(13,150)	(13,981)	(17,813)	(23,818)	(22,976)	(22,809)	(21,307)
Exceptionals including asset impairment	74	18	41	1,205	0	0	0
Operating Profit	(13,077)	(13,964)	(17,771)	(22,613)	(22,976)	(22,809)	(21,307)
Net Interest	(883)	(878)	(1,178)	(608)	(364)	(1,382)	(3,484)
Profit Before Tax (norm)	(14,033)	(14,859)	(18,991)	(24,426)	(23,340)	(24,191)	(24,792)
Profit Before Tax (FRS 3)	(13,960)	(14,841)	(18,949)	(23,221)	(23,340)	(24,191)	(24,792)
Tax	(24)	(136)	(157)	(393)	0	0	0
Profit After Tax and minority interests (norm)	(14,057)	(14,995)	(19,148)	(24,819)	(23,340)	(24,191)	(24,792)
Profit After Tax and minority interests (FRS 3)	(13,983)	(14,977)	(19,106)	(23,614)	(23,340)	(24,191)	(24,792)
Average Number of Shares Outstanding (m)	10.0	12.3	15.3	18.2	23.8	23.8	23.9
EPS - normalised (€)	(1.41)	(1.22)	(1.25)	(1.36)	(0.98)	(1.01)	(1.04)
EPS - normalised and fully diluted (€)	(1.41)	(1.22)	(1.25)	(1.36)	(0.98)	(1.01)	(1.04)
EPS - (IFRS) (€)	(1.40)	(1.22)	(1.25)	(1.30)	(0.98)	(1.01)	(1.04)
Dividend per share (€)	0.0	0.0	0.0	0.0	0.0	0.0	0.0
BALANCE SHEET							
Fixed Assets	242	829	772	1,814	1,617	1,517	1,876
Tangible Assets	184	765	705	1,732	1,535	1,435	1,794
Investments in long-term financial assets	58	63	67	82	82	82	82
Current Assets	3,099	8,522	13,441	12,890	14,229	15,189	16,056
Short-term investments	0	0	0	0	0	0	0
Cash	1,318	5,586	11,016	9,600	13,568	14,883	14,375
Other	1,782	2,935	2,425	3,290	661	307	1,680
Current Liabilities	(18,727)	(5,315)	(5,966)	(7,180)	(3,546)	(3,039)	(3,487)
Creditors	(6,654)	(4,855)	(5,966)	(7,180)	(3,546)	(3,039)	(3,487)
Short term borrowings	(12,073)	(459)	0	0	0	0	0
Long Term Liabilities	(3,374)	(3,110)	(8,135)	(8,312)	(8,312)	(33,312)	(58,312)
Long term borrowings	(2,582)	(2,261)	(7,473)	(7,325)	(7,325)	(32,325)	(57,325)
Other long-term liabilities	(792)	(849)	(662)	(987)	(987)	(987)	(987)
Net Assets	(18,760)	926	113	(788)	3,989	(19,645)	(43,868)
CASH FLOW							
Operating Cash Flow	(8,987)	(17,596)	(15,791)	(22,786)	(22,998)	(22,027)	(21,318)
Net interest and financing income (expense)	(883)	(878)	(1,178)	(608)	(364)	(1,382)	(3,484)
Tax	(5)	(9)	(36)	(222)	0	0	0
Net Operating Cash Flow	(9,875)	(18,482)	(17,005)	(23,616)	(23,362)	(23,409)	(24,802)
Capex	(39)	(106)	(138)	(326)	(240)	(276)	(706)
Acquisitions/disposals	0	0	0	0	0	0	0
Financing (net of costs)	2	26,165	19,000	22,771	27,567	0	0
Dividends	0	0	0	0	0	0	0
Other	0	0	0	0	0	0	0
Net Cash Flow	(9,912)	7,576	1,857	(1,171)	3,966	(23,685)	(25,507)
Opening net debt/(cash)	0	13,337	(2,866)	(3,543)	(2,275)	(6,243)	17,442
HP finance leases initiated	0	0	0	0	0	0	0
Other	(3,425)	8,627	(1,179)	(97)	0	0	(0)
Closing net debt/(cash)	13,337	(2,866)	(3,543)	(2,275)	(6,243)	17,442	42,950
Lease debt	N/A	504	387	760	760	760	760
Closing net debt/(cash) inclusive of IFRS 16 lease debt	13,337	(2,362)	(3,157)	(1,515)	(5,483)	18,202	43,710

Source: Company data, Edison Investment Research

Contact details	Revenue by geography
Sequana Medical NV Technologiepark 122 9052 Zwijnaarde Belgium +32 9 292 8065 www.sequanamedical.com	

Management team

Chief executive officer: Ian Crosbie

Ian has served as CEO since 2016 and has been a member of the board of directors since 2019. Ian has over 25 years of experience in the healthcare sector, both in-house at medical device and pharmaceutical companies, and as an investment banker at several global firms. He has significant experience in implantable medical devices as well as in capital markets, licensing and strategic transactions. Prior to joining Sequana Medical, Ian was chief financial officer of GC Aesthetics based in Dublin. Before that, Ian was senior vice-president, corporate development at Circassia Pharmaceuticals, a late-stage biopharmaceutical company focused on allergy immunotherapy, where he oversaw the execution of the company's £210m IPO, as well as M&A and licensing activities. Prior to Circassia, Ian had a 20-year career in corporate finance, including managing director, healthcare investment banking at Jefferies International and director, healthcare investment banking at Deutsche Bank. He has a degree in engineering, economics and management from Oxford University.

Chief financial officer: Kirsten Van Bockstaele

Kirsten is a seasoned finance executive with over 20 years of international experience in the healthcare industry. Before joining Sequana Medical, Kirsten was vice-president of finance at Fagron, North America, where she was responsible for creating and overseeing the company's financial strategy and policy and positioning Fagron's North American companies for growth. Before that, Kirsten served as chief financial officer for Arseus Dental & Medical Solutions, where she held a key role in the coordination, support and control of financial activities in key European countries. Her previous roles include financial controller at Omega Pharma and audit manager at PwC. Kirsten has a degree in business economics from EHSAL and a degree in financial and fiscal sciences from the University of Antwerp, Belgium.

Chief medical officer: Oliver Gödje

Oliver is an experienced clinician and medtech industry executive with 18 years of international experience in medical and commercial roles. Prior to joining Sequana Medical, Oliver served as chief medical officer at Humedic, medical director and VP sales & marketing at Hepa Wash, chief medical officer and chief marketing officer at Tensys Medical, and medical & marketing director of PULSION Medical Systems, all medtech companies in the liver or cardiovascular field. He holds a PhD and professorship in human medicine and built an extensive knowledge of cardiology during his time as a cardiac surgeon at leading German universities. He was a consultant and vice-chairman of the Department of Cardiac Surgery at the University Hospital of Ulm until 2002.

Global vice-president, QM/QA/RA: Timur Resch

Timur has 10 years of experience within quality management and regulatory affairs in the regulated medical device industry. In 2010, Timur graduated as an engineer in medical technology from the University of Applied Sciences in Lübeck, Germany, and began his professional career as a process and management consultant at Synspace. Thereafter, Timur continued as head of quality management & regulatory affairs at Schaerer Medical and prior to joining Sequana Medical held the position of manager & team leader regulatory affairs at Medela. His experience includes the establishment of quality management systems, auditing, international product registrations for Class I to Class III medical devices, ensuring compliance with applicable regulatory requirements as well as being the liaison to notified bodies and health authorities. Timur serves as member of quality and regulatory task forces and expert groups within Germany and Switzerland.

Principal shareholders	(%)
Neomed	18.1
PiEquity	15.3
LSP	8
SFPI-FPIM	7.3
PMV	7
Newton Biocapital	4.6
GRAC	4.2
Belfius Insurance	4.2

General disclaimer and copyright

This report has been commissioned by Sequana Medical and prepared and issued by Edison, in consideration of a fee payable by Sequana Medical. Edison Investment Research standard fees are £60,000 pa for the production and broad dissemination of a detailed note (Outlook) following by regular (typically quarterly) update notes. Fees are paid upfront in cash without recourse. Edison may seek additional fees for the provision of roadshows and related IR services for the client but does not get remunerated for any investment banking services. We never take payment in stock, options or warrants for any of our services.

Accuracy of content: All information used in the publication of this report has been compiled from publicly available sources that are believed to be reliable, however we do not guarantee the accuracy or completeness of this report and have not sought for this information to be independently verified. Opinions contained in this report represent those of the research department of Edison at the time of publication. Forward-looking information or statements in this report contain information that is based on assumptions, forecasts of future results, estimates of amounts not yet determinable, and therefore involve known and unknown risks, uncertainties and other factors which may cause the actual results, performance or achievements of their subject matter to be materially different from current expectations.

Exclusion of Liability: To the fullest extent allowed by law, Edison shall not be liable for any direct, indirect or consequential losses, loss of profits, damages, costs or expenses incurred or suffered by you arising out or in connection with the access to, use of or reliance on any information contained on this note.

No personalised advice: The information that we provide should not be construed in any manner whatsoever as, personalised advice. Also, the information provided by us should not be construed by any subscriber or prospective subscriber as Edison's solicitation to effect, or attempt to effect, any transaction in a security. The securities described in the report may not be eligible for sale in all jurisdictions or to certain categories of investors.

Investment in securities mentioned: Edison has a restrictive policy relating to personal dealing and conflicts of interest. Edison Group does not conduct any investment business and, accordingly, does not itself hold any positions in the securities mentioned in this report. However, the respective directors, officers, employees and contractors of Edison may have a position in any or related securities mentioned in this report, subject to Edison's policies on personal dealing and conflicts of interest.

Australia

Edison Investment Research Pty Ltd (Edison AU) is the Australian subsidiary of Edison. Edison AU is a Corporate Authorised Representative (1252501) of Crown Wealth Group Pty Ltd who holds an Australian Financial Services Licence (Number: 494274). This research is issued in Australia by Edison AU and any access to it, is intended only for "wholesale clients" within the meaning of the Corporations Act 2001 of Australia. Any advice given by Edison AU is general advice only and does not take into account your personal circumstances, needs or objectives. You should, before acting on this advice, consider the appropriateness of the advice, having regard to your objectives, financial situation and needs. If our advice relates to the acquisition, or possible acquisition, of a particular financial product you should read any relevant Product Disclosure Statement or like instrument.

New Zealand

The research in this document is intended for New Zealand resident professional financial advisers or brokers (for use in their roles as financial advisers or brokers) and habitual investors who are "wholesale clients" for the purpose of the Financial Advisers Act 2008 (FAA) (as described in sections 5(c) (1)(a), (b) and (c) of the FAA). This is not a solicitation or inducement to buy, sell, subscribe, or underwrite any securities mentioned or in the topic of this document. For the purpose of the FAA, the content of this report is of a general nature, is intended as a source of general information only and is not intended to constitute a recommendation or opinion in relation to acquiring or disposing (including refraining from acquiring or disposing) of securities. The distribution of this document is not a "personalised service" and, to the extent that it contains any financial advice, is intended only as a "class service" provided by Edison within the meaning of the FAA (i.e. without taking into account the particular financial situation or goals of any person). As such, it should not be relied upon in making an investment decision.

United Kingdom

This document is prepared and provided by Edison for information purposes only and should not be construed as an offer or solicitation for investment in any securities mentioned or in the topic of this document. A marketing communication under FCA Rules, this document has not been prepared in accordance with the legal requirements designed to promote the independence of investment research and is not subject to any prohibition on dealing ahead of the dissemination of investment research.

This Communication is being distributed in the United Kingdom and is directed only at (i) persons having professional experience in matters relating to investments, i.e. investment professionals within the meaning of Article 19(5) of the Financial Services and Markets Act 2000 (Financial Promotion) Order 2005, as amended (the "FPO") (ii) high net-worth companies, unincorporated associations or other bodies within the meaning of Article 49 of the FPO and (iii) persons to whom it is otherwise lawful to distribute it. The investment or investment activity to which this document relates is available only to such persons. It is not intended that this document be distributed or passed on, directly or indirectly, to any other class of persons and in any event and under no circumstances should persons of any other description rely on or act upon the contents of this document.

This Communication is being supplied to you solely for your information and may not be reproduced by, further distributed to or published in whole or in part by, any other person.

United States

Edison relies upon the "publishers' exclusion" from the definition of investment adviser under Section 202(a)(11) of the Investment Advisers Act of 1940 and corresponding state securities laws. This report is a bona fide publication of general and regular circulation offering impersonal investment-related advice, not tailored to a specific investment portfolio or the needs of current and/or prospective subscribers. As such, Edison does not offer or provide personal advice and the research provided is for informational purposes only. No mention of a particular security in this report constitutes a recommendation to buy, sell or hold that or any security, or that any particular security, portfolio of securities, transaction or investment strategy is suitable for any specific person.

Frankfurt +49 (0)69 78 8076 960
Schumannstrasse 34b
60325 Frankfurt
Germany

London +44 (0)20 3077 5700
280 High Holborn
London, WC1V 7EE
United Kingdom

New York +1 646 653 7026
1185 Avenue of the Americas
3rd Floor, New York, NY 10036
United States of America

Sydney +61 (0)2 8249 8342
Level 4, Office 1205
95 Pitt Street, Sydney
NSW 2000, Australia