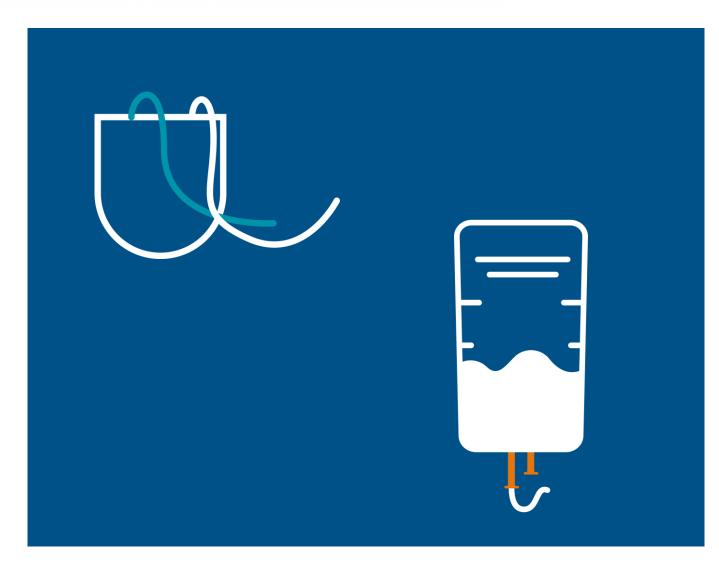
### **sequana** medical



### Pioneers in the treatment of fluid overload

liver disease, heart failure & cancer

Investor presentation – January 2023 Euronext: SEQUA.BR

### **Disclaimers**

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#### **Regulatory disclaimer:**

- The alfapump<sup>®</sup> system has not yet received regulatory approval in the United States and Canada. Any statement in this presentation about safety and efficacy of the alfapump<sup>®</sup> system does not apply to the United States and Canada. In the United States and Canada, the alfapump<sup>®</sup> 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 visit <u>www.poseidonstudy.com</u>.
- DSR<sup>®</sup> therapy is still under 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. DSR<sup>®</sup> therapy is currently
  not approved for clinical research in the United States or Canada. There is no link between DSR<sup>®</sup> therapy and
  ongoing investigations with the alfapump<sup>®</sup> system in Europe, the United States or Canada.

#### COVID-19 disclaimer:

- Sequana Medical is closely following the evolution of the COVID-19 global health crisis and is in constant dialogue with its partners to assess the impact and adapt operations accordingly.
- Sequana Medical has put in place mitigation plans to minimise delays. The impact of increased demands on the healthcare systems, limitations on non-essential hospital visits and procedures, social-distancing and travel restrictions may result in further delays to execution of clinical studies and impact sales.
- Sequana Medical will continue to update the market as needed and whenever possible.

#### Note:

 alfapump<sup>®</sup> is a registered trademark. DSR<sup>®</sup> is a registered trademark in the Benelux, China, the EU, United Kingdom, and Hong Kong.

### Leading player in the treatment of fluid overload

- Proprietary technologies meeting large and unmet clinical needs
  - Key clinical problem in liver disease, heart failure, renal failure and cancer
  - We are not replacing diuretics we are targeting those patients for whom they are not effective
  - Diuretic-resistance is common and alternative treatments have significant disadvantages
- Strong granted IP portfolio
- alfapump<sup>®</sup> in liver disease market potential growing to over \$2 billion by 2032<sup>(1)</sup>
  - NASH is changing liver cirrhosis market and driving growth
  - Approved in EU / FDA breakthrough designation in US
  - North American pivotal study met all primary effectiveness endpoints with statistical significance and primary safety endpoint data in line with expectations
  - Direct commercialization in US through salesforce targeting liver transplant centres

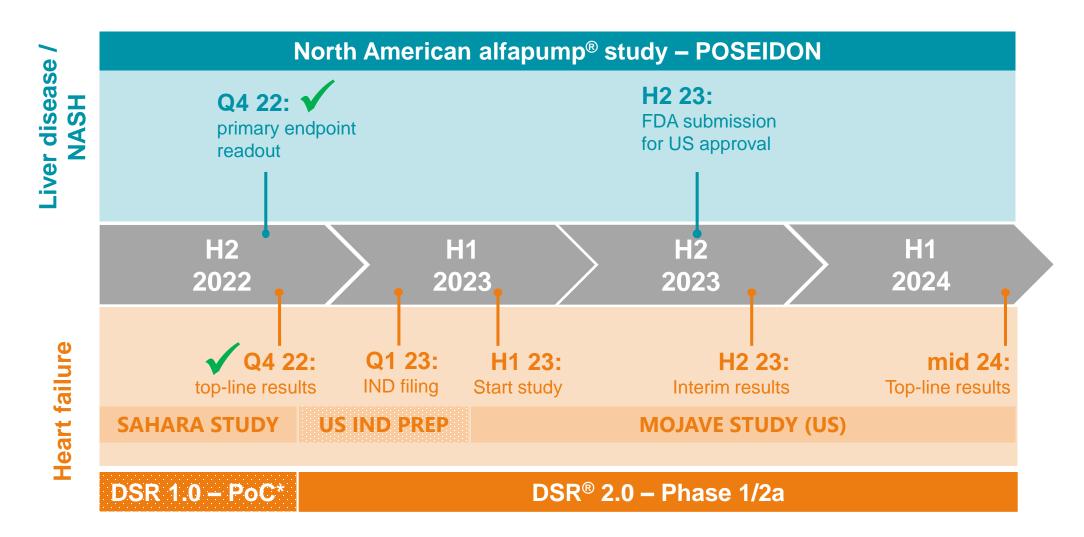


- DSR<sup>®</sup> in heart failure multi-billion market opportunity
  - Disease-modifying heart failure drug therapy; short course of therapy
  - 1<sup>st</sup> generation DSR 1.0 clinical proof-of-concept
  - 2<sup>nd</sup> generation DSR 2.0 strong IP, preparing US IND to start MOJAVE (Ph. 1/2 study in H1 '23)
  - Establish partnership based on MOJAVE readout

Source 1: Based on US and Canada market assessment conducted by highly experienced international consulting group, estimating over 140,000 patients with recurrent or refractory ascites in North America by 2032, with estimated incidence of 60% and based on \$25K for price of **alfa**pump **IP**: Intellectual Property; **IND**: Investigational New Drug



### **Strong outlook for value drivers**



Note: Description and timing of these studies are subject to change and/or feedback from applicable regulatory authorities



# alfapump®

Proven step change in the treatment of liver refractory ascites

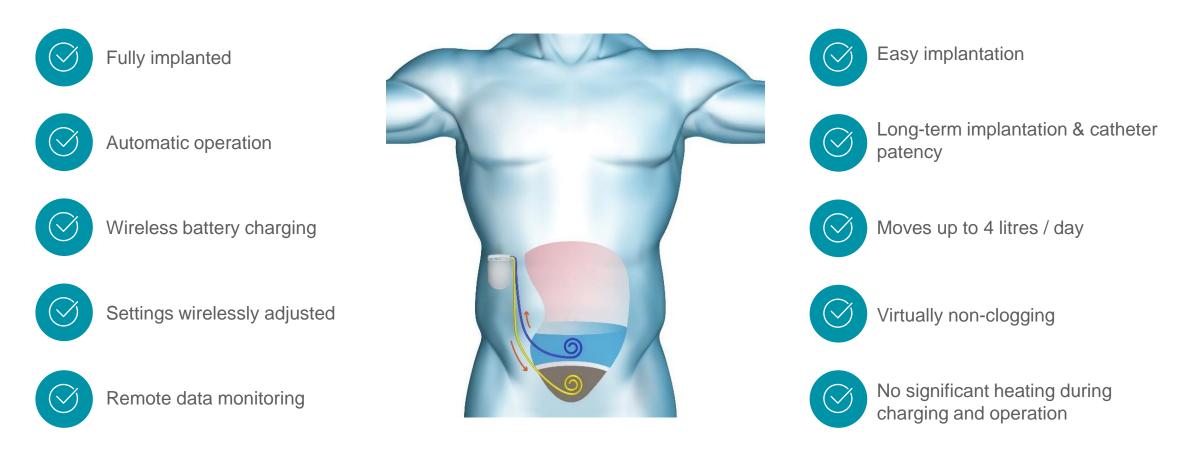


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Proven capabilities – over 950 systems implanted Strong IP barriers through extensive patent portfolio & know-how

### alfapump

Eliminating fluid from the peritoneal cavity – working in partnership with the bladder

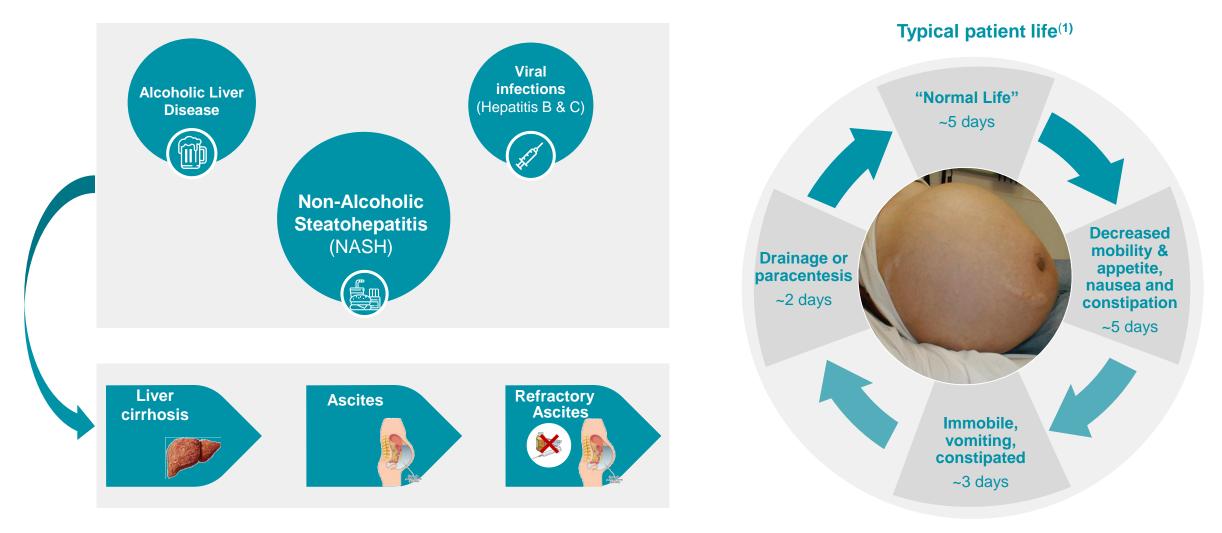




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### **Refractory ascites – key complication of liver cirrhosis**

Fatty liver disease / NASH is driving dramatic growth and change in attitudes to liver cirrhosis patients



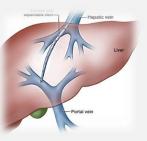
### **Limitations of existing therapies**

#### Drainage ("Large Volume Paracentesis / LVP")



Painful, Poor Quality of Life, Short Term Benefit

#### **Transjugular Intrahepatic Portosystemic Shunt (TIPS)**



Complications, Contraindications

### alfapump



#### **Permanent Catheter System**

### Liver transplantation



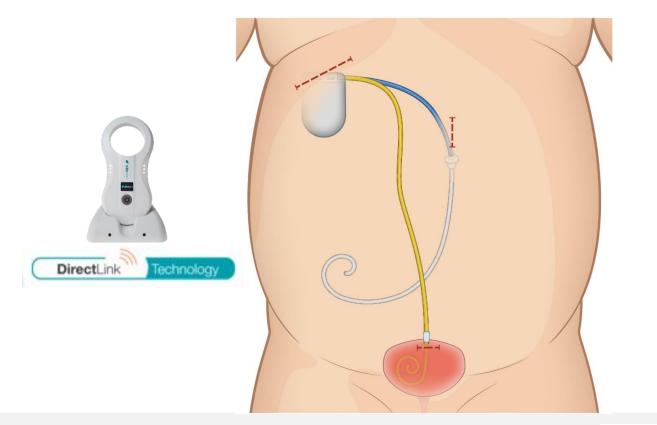
External Catheter, Risk for Infections / Blockage

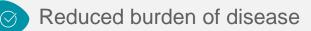


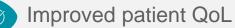
High Cost, Limited Availability

### alfapump strong clinical and economic rationale

Over 950 implants and hundreds of years of patient experience







Cost savings for hospitals and payers

Estimated treatment cost / patient\*:

LVP: ~\$43K

alfapump®: ~\$35K

~\$1.8K / LVP<sup>(1)</sup> 1 LVP / month 24 months ~\$25K / **alfa**pump ~\$10K / implantation

\* Management estimate of US treatment costs, assuming no complications QoL: Quality of Life; LVP: Large Volume Paracentesis





NICE National Institute for Health and Care Excellence

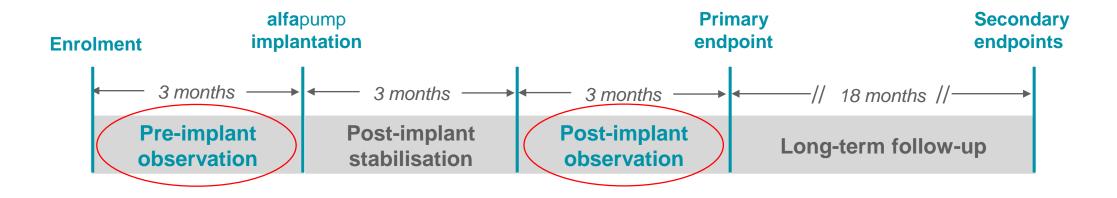




Breakthrough Device Designation

### **POSEIDON – North American pivotal study**

Pivotal Cohort of 40 patients implanted with the alfapump



**POSEIDON** primary effectiveness endpoint hypotheses:

 median per-patient ratio of post-implant three-month observation period to the pre-implant three-month observation period with respect to number of therapeutic paracentesis (TP) is less than 0.5 (or a median reduction of at least 50%)
 at least 50% of patients achieve a 50% reduction in the requirement for TP in the same period

### **POSEIDON: Primary effectiveness endpoints met**

Results substantially exceeded the predefined thresholds for study success

Pivotal Cohort N = 40	%*	p-value**
<ol> <li>Frequency of Therapeutic Paracentesis (TP)         <ul> <li>a. median per-patient ratio</li> <li>b. mean per-patient ratio</li> </ul> </li> </ol>	100% reduction 82% reduction	P<0.001 Not applicable
2. Proportion of patients with a 50% reduction in number of TP post- vs pre-implantation	77% of patients	P<0.001

"These positive top-line results are very encouraging, indicating that the alfapump could provide great benefits to patients with cirrhosis and ascites, and dramatically reduce their visits to the hospital for paracentesis." – Dr. Wong, Principal Investigator POSEIDON

\* Using pre-specified imputation methods for 14 patients that had exited the study prior to completing the 6-month post-implantation period.

\*\* As per primary effectiveness endpoint hypotheses. Per protocol, testing conducted using nonparametric methods for data that is not normally distributed.

# **POSEIDON: Primary safety endpoint in line with expectations**

#### Primary safety endpoint (pivotal cohort N = 40):

- Combined rate of i) open surgical re-intervention due to pump system-related AE or to restore pump functionality, ii) pump explant (without replacement) due to pump system-related AE, or iii) pump system-related death from time of pump implant through 6 months post-implantation as adjudicated by the CEC
- No unanticipated adverse device effects
- Six primary safety events in line with expectations:
  - Wound erosion alfapump explant
     3 in 3 patients
  - Patient-reported discomfort **alfa**pump explant

3 in 3 patients

CEC: moderate severity

"The safety data regarding the primary safety endpoint are in line with expectations and reassuring for the potential of the alfapump as a long-term treatment in this patient population" – Dr. Wong, Principal Investigator POSEIDON

### North American alfapump approval expected in 2024

2022	2023	2024
O O Completion ✓ Primary ✓ alfapump endpoint implants readout	POSEIDON	C Secondary endpoint readout
	<b>★</b> PMA submission	<b>★</b> US Launch
US Commercial Scale-Up	Head of N. America	Clinical Sales specialists Reps

NTAP for breakthrough devices de-risks reimbursement in key Medicare population\*

\*On the basis of existing ICD-10 codes issued for the alfapump, the likely DRG coding will be 423, 424 and 425 "OTHER HEPATOBILIARY OR PANCREAS O.R. PROCEDURES"

PMA: Pre-Market Approval; NTAP: New Technology Add-On Payment

### Large and growing North American patient population

NASH is forecast to drive significant growth for many years – and changing attitudes to cirrhosis

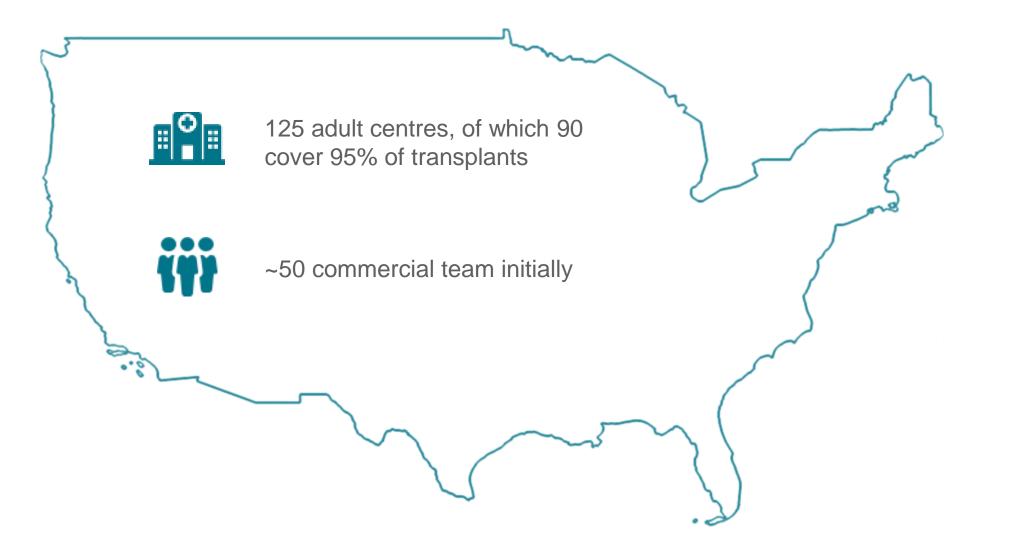


- NASH is a key driver of growth, with alcohol continuing to play an important role
- Estimated incidence of 60%
- Market potential growing to over \$2 billion by 2032\*
- US and Canada market assessment conducted by highly experienced international consulting group
  - Claims analysis for commercial and CMS patients requiring paracentesis procedure with liver disease diagnosis codes



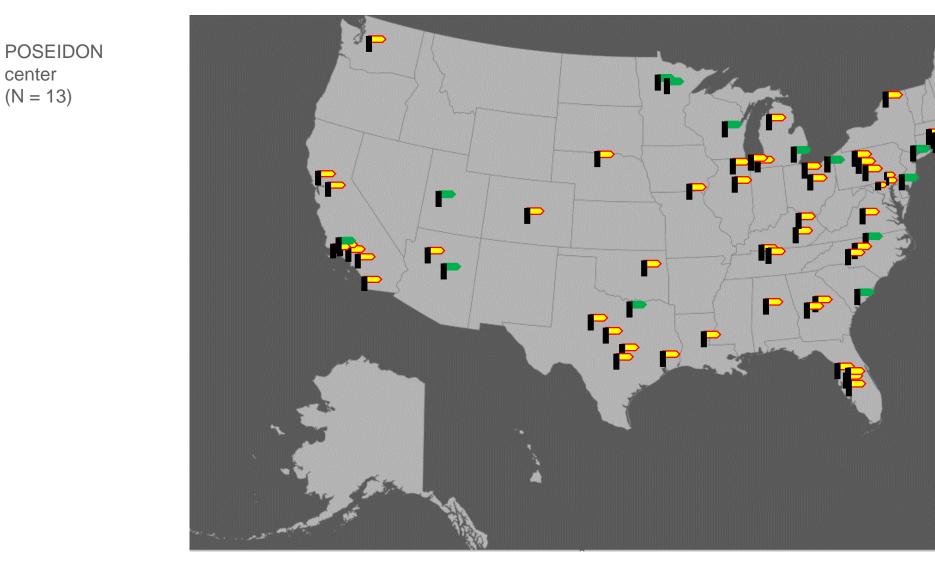
### **US – Go direct to 90 liver transplant centers**

Highly efficient approach to target doctors and patients – driven by treatment guidelines



### **Top 60 liver transplant centers (2021)**

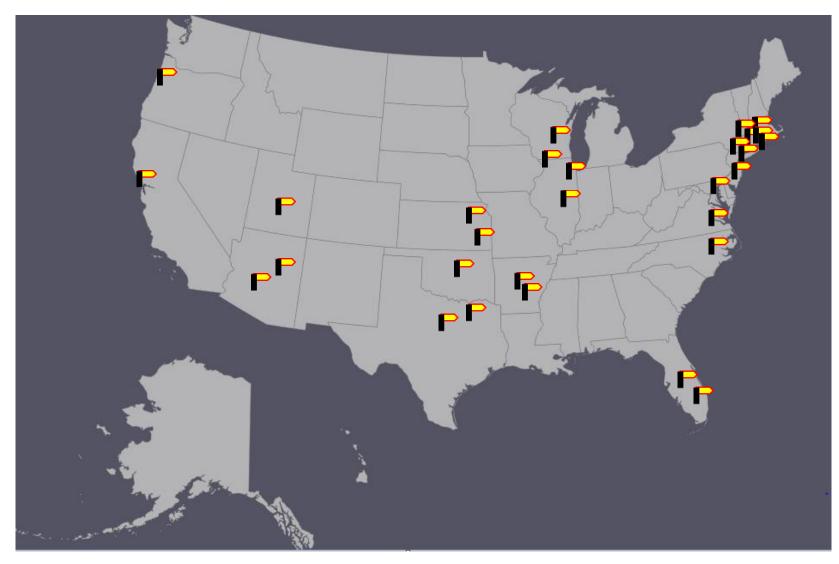
Top 60 centers cover 80% of transplants (6,967 out of 8,685)





### **Top 61 – 90 liver transplant centers (2021)**

30 centers cover 15% of transplants (1,347 out of 8,685)





# **DSR**<sup>®</sup>

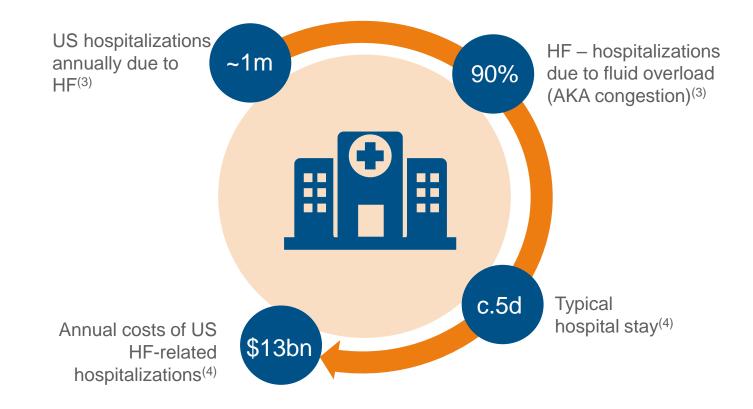
### Disease-modifying heart failure drug therapy



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### **Congestion is driver of morbidity and hospitalization**

Diuretic-resistance is common and there are few effective clinical alternatives



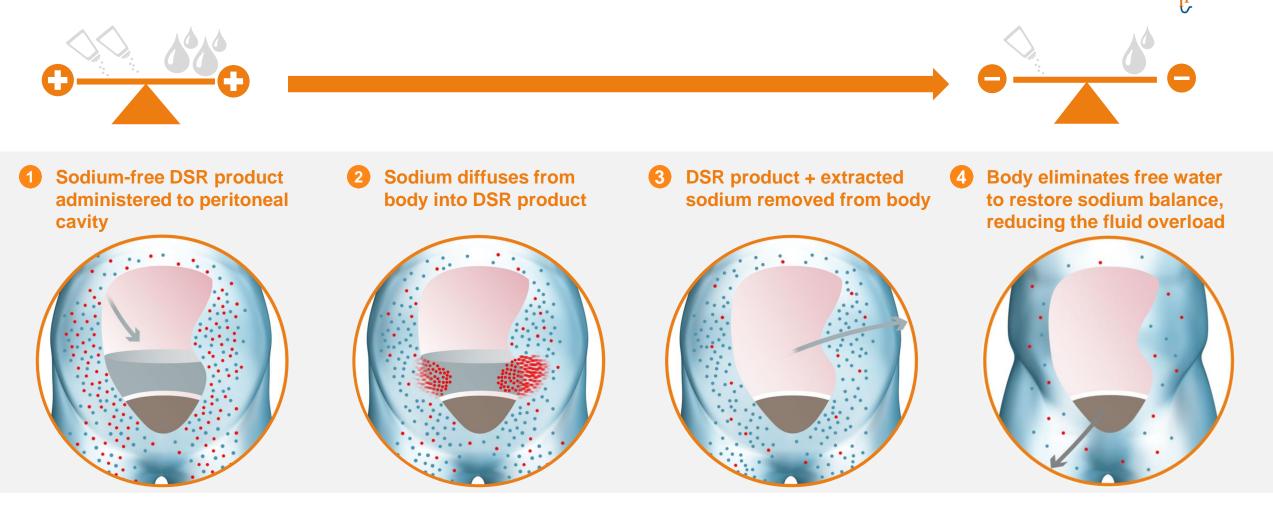
- 40% of heart failure patients on IV loop diuretics have a poor response<sup>(1)</sup>
- 24% re-admission rate at 30 days<sup>(2)</sup>

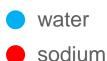
Source 1: Testani, Circ Heart Failure, 2014 & 2016; Source 2: Ross et al. (2010); Source 3: Costanzo et al., J. Am. Coll., 2007; Source 4: Kilgore et al. (2017)

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# **Direct Sodium Removal (DSR)**

Eliminating fluid spread across the body – working in partnership with the kidneys





Fundamental patents to reduce fluid overload in heart failure patients granted in the US and Europe

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### **RED DESERT: Successful proof-of-concept study**

8 euvolemic HF patients on high dose diuretics treated with DSR 3x per week up to 6 weeks

### Highly effective management of fluid and sodium balance

• Generally safe and well tolerated; no clinically relevant hyponatremia

### **Significant improvement in cardio-renal status**

- 30% decrease\* in NT-proBNP\*\* (p<0.001)
- 22% increase\* in eGFR\*\* (p<0.001)

#### **Dramatic and sustained improvement in diuretic response**\*\*\*

• Over 150% increase\*\* in six hour excretion of sodium

### No congestion-related heart failure re-hospitalizations

"Simultaneous normalization of diuretic response and improvement in cardio-renal status is a never before seen treatment effect" – Dr. Testani, Yale

\* Paired statistical analysis of patients with baseline and D42 value (N=7); \*\* mean value; \*\*\*assessed by 6-hour excretion of sodium after IV administration of 40mg furosemide **NT-proBNP**: N-terminal-pro hormone B-type Natriuretic Peptide (analysed in local lab); **eGFR**: estimated glomerular filtration rate



### **SAHARA: Expanding into decompensated patients**

10 evaluable diuretic-resistant HF patients with persistent congestion on 2-6 weeks of intensive DSR therapy<sup>1</sup>

#### Safely, effectively and rapidly eliminate persistent congestion & restore euvolemia

- All patients achieved euvolemia within one week of intensive DSR therapy
- Weight loss\* of 7kg vs. baseline at end of intensive DSR therapy & no clinically relevant hyponatremia

#### **Considerably benefit cardio-renal status**

- More than 30% reduction\* in NT-proBNP
- Stable eGFR despite dramatic fluid loss

#### **Dramatic and sustained improvement in diuretic response\*\***

• End of intensive DSR therapy: more than 160% increase\* (near normal levels)

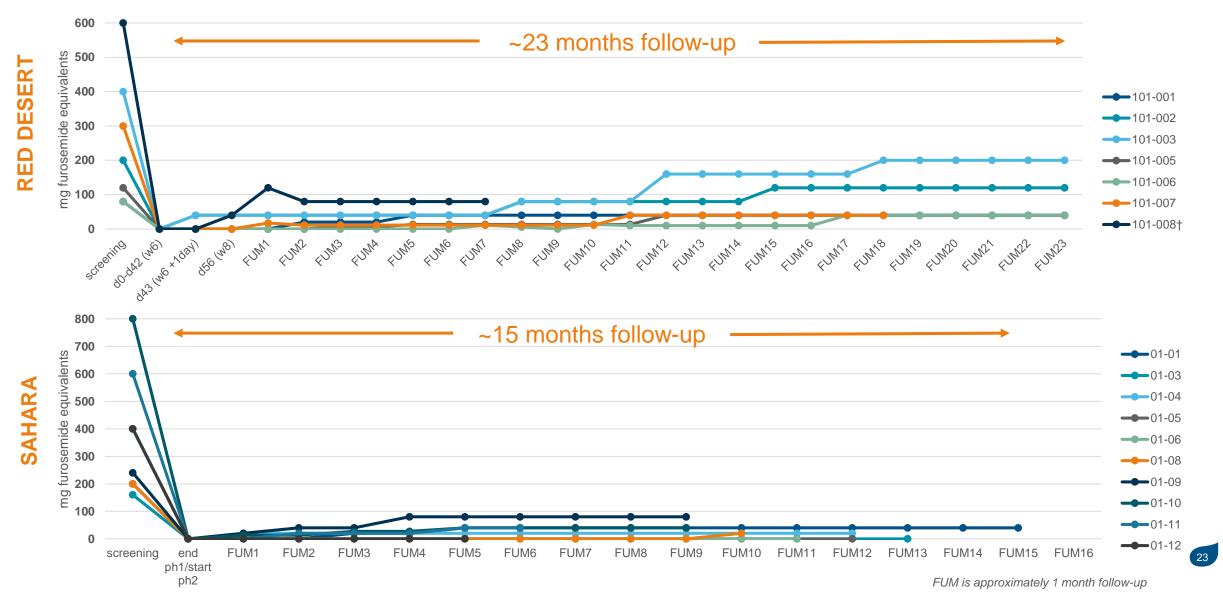
#### No congestion-related heart failure re-hospitalizations

"The SAHARA results are highly encouraging and indicate the potential for DSR therapy to deliver clinically meaningful decongestion and durable improvements in cardio-renal function and thus diuretic response" – Dr. Testani, Yale

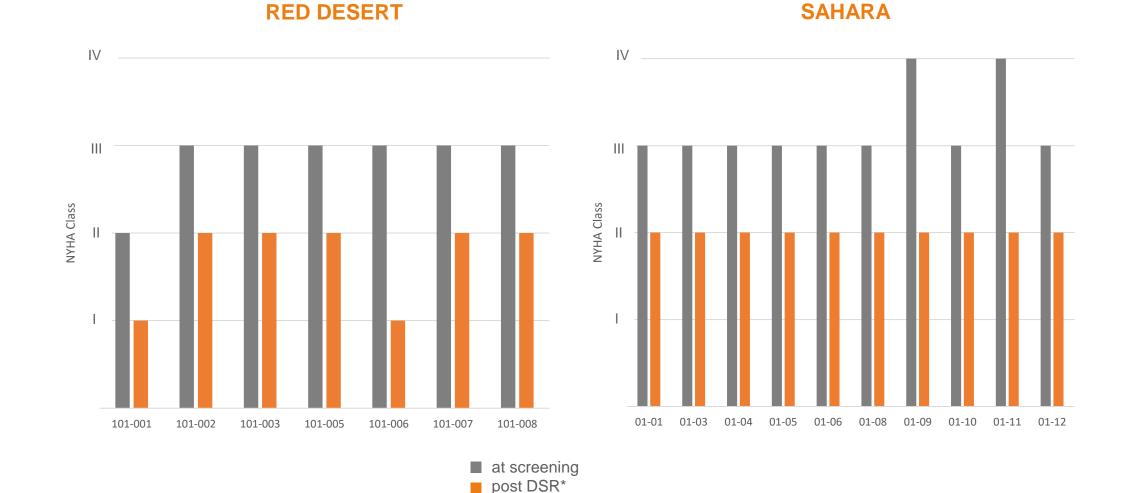
<sup>1</sup> two additional patients were dosed but one patient died due to a cardiac arrest three days after study initiation and for one patient the study protocol was not correctly applied \*mean value; \*\* assessed by 6-hour excretion of sodium after IV administration of 40mg furosemide; **NT-proBNP**: N-terminal-pro hormone B-type Natriuretic Peptide (analysed in local lab); **eGFR**: estimated glomerular filtration rate

### Long-term & major reduction in loop diuretic dosing

Clear demonstration of improvement in cardio-renal health – driving improved clinical outcomes



### **Consistently improved NYHA class at least one level**



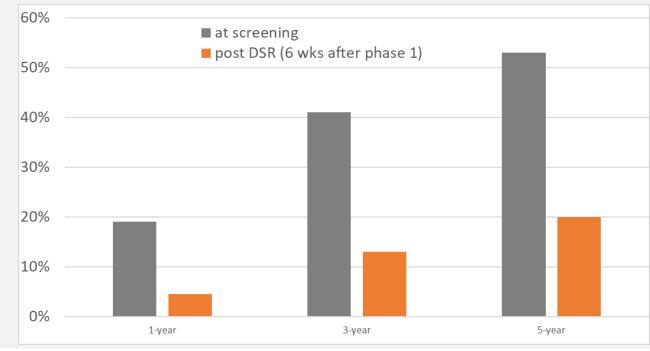
\* Post DSR = end of phase 1 (6w) in RED DESERT and day 42 in SAHARA

Note: data on NYHA classification collected outside study protocols of RED DESERT and SAHARA

### **Strong reduction in predicted mortality**

Over 75% reduction in predicted one-year mortality based on Seattle Heart Failure Model\*

- Seattle Heart Failure Model is a highly validated model to predict survival in heart failure
  - Validated in approx. 10,000 heart failure patients in over 46 countries with >17,000 person-years follow-up
  - Excellent accuracy, with predicted vs. actual one-year survival rate of respect. 90.5% vs. 88.5%-
- Substantial reduction in overall predicted mortality post DSR\* vs. screening, at 1y, 3y and 5y:



\* Predicted one-year survival analysis using Seattle Heart Failure Model with seven patients from RED DESERT and ten patients from SAHARA pre- and post-intensive DSR therapy. Analysis includes physician-assessed data collected post hoc.

\*\* Post DSR = 6 weeks after phase 1 (phase 1 = 6<sup>th</sup> week in RED DESERT; 2<sup>nd</sup>, 4<sup>th</sup> or 6<sup>th</sup> week in SAHARA)

Sequana

Polydextrin + Dextrose

### **DSR 2.0 has improved therapeutic and safety profile**

Strong granted IP drives high margin recurring revenue stream

#### DSR 1.0 Sodium-free D10% (off-the-shelf)

- Clinical proof-of-concept
- Rapid clinical path
- Therapeutic profile / Ease of use
- Safety profile

#### Sodium-free dextrose / icodextrin (proprietary)

**DSR 2.0** 

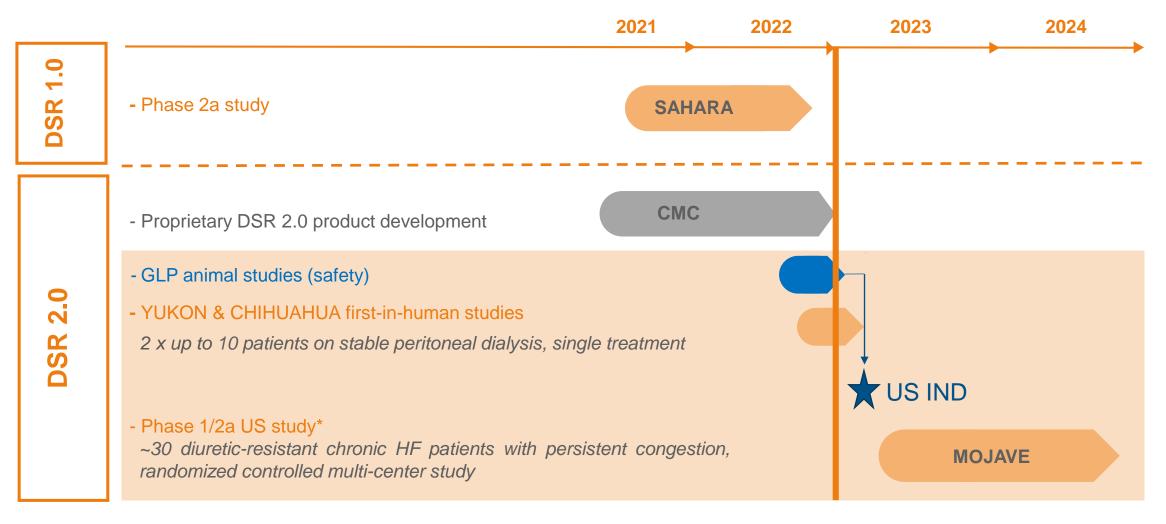
- Improved therapeutic profile
- ✓ Favorable safety profile
- Strong granted IP position in US & Europe
  - "Low or no sodium drug for the treatment of heart failure"
  - Drives recurring revenue from high gross margin consumable
- First-in-human insights with single DSR treatment in up to 20 patients – safety and dosing
- Preparations US IND filing ongoing to start Phase 1/2a MOJAVE study in H1 2023

#### YUKON – CHIHUAHUA – MOJAVE

### RED DESERT – SAHARA

### **MOJAVE as package for DSR partnering**

Leveraging the strengths of established HF player to realise commercial potential of DSR



\* Description and timing of this study is subject to change and/or feedback from applicable regulatory authorities

**GLP**: Good Laboratory Practice

### **Multi-billion market opportunity**

Delivering value through reduced hospitalization and improved survival

- ~400K chronically congested HF patients hospitalized per year in the US and EU ("frequent flyers")
  - High cost patients with major burden on healthcare systems, payors and patients
- Value based pricing of DSR drug driven by:
  - ⇒ Reduction in re-hospitalization ~\$40K annual HF hospitalization cost per patient
  - ⇒ Increase in survival (gain in quality-adjusted life-year, "QALY")

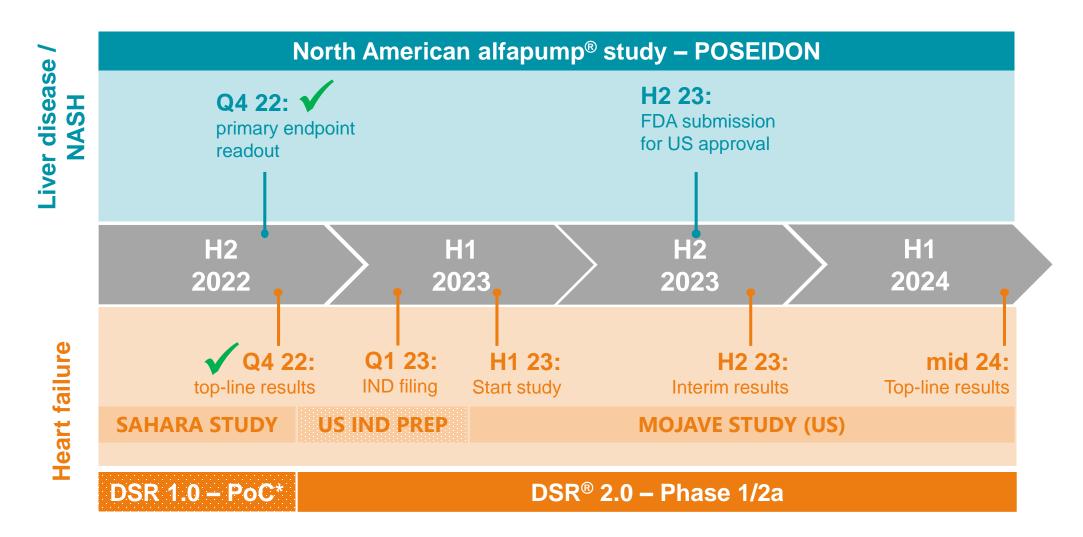


### Outlook

Strong near term value drivers with clear long term potential

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### **Strong outlook for value drivers**



Note: Description and timing of these studies are subject to change and/or feedback from applicable regulatory authorities

\* PoC: Clinical Proof-of-Concept

### Leader in large and growing markets with unmet needs

#### alfapump<sup>®</sup> in liver disease – market potential growing to over \$2 billion by 2032<sup>(1)</sup>

- NASH is changing liver cirrhosis market and driving strong growth
- FDA breakthrough device status / Strong IP portfolio
- North American pivotal study reported strong primary endpoint data
- North American approval expected in 2024 / Go direct to 140 liver transplant centres

#### DSR<sup>®</sup> in heart failure – multi-billion market opportunity

- Disease-modifying heart failure drug therapy
- Clinical proof-of-concept with DSR 1.0 Important and durable clinical benefits
- Transitioning to proprietary DSR 2.0 Low development risk, improved profile & strong IP
- Establish partnership based on MOJAVE; Phase 1/2a randomized controlled US study

Source 1: Based on US and Canada market assessment conducted by highly experienced international consulting group, estimating over 140,000 patients with recurrent or refractory ascites in North America by 2032, with estimated incidence of 60% and based on \$25K for price of **alfa**pump

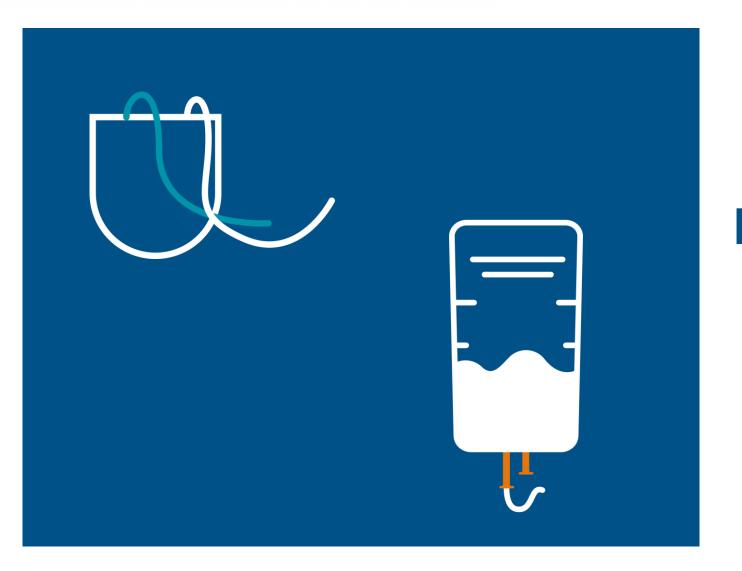
### **Contact info**

IR@sequanamedical.com +32 498 053579

www.sequanamedical.com

sequana medical

## **sequana** medical



### **Back-up**

### **Sequana Medical NV**

#### Founded in 2006

Gent, Belgium (HQ): corporate, clinical, commercial

Zurich, Switzerland: manufacturing, engineering, QA/RA

>60 employees

Euronext Brussels: SEQUA



### **Strong organisation**

Highly experienced leadership team supported by committed and well-reputed shareholders

#### **Executive team:**



lan Crosbie Chief Executive Officer



Kirsten Van Bockstaele Chief Financial Officer



**Oliver Gödje** Chief Medical Officer



Dragomir Lakic VP Manufacturing



Gijs Klarenbeek Senior Medical Advisor



Martijn Blom Chief Commercial Officer



Timur Resch Global VP QM/QA/RA



Andreas Wirth VP Engineering

#### **Board of Directors:**



Pierre Chauvineau Board Chairman



lan Crosbie Chief Executive Officer



Wim Ottevaere Director



Jackie Fielding Director



Rudy Dekeyser Director



Doug Kohrs Director

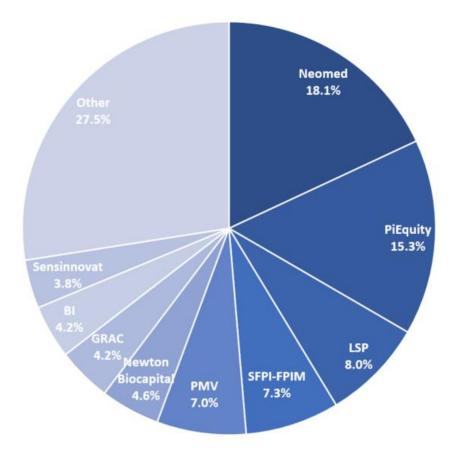


Alex Clyde Director

### **Shareholders base and financial overview**

**Ticker: SEQUA – Euronext Brussels** 

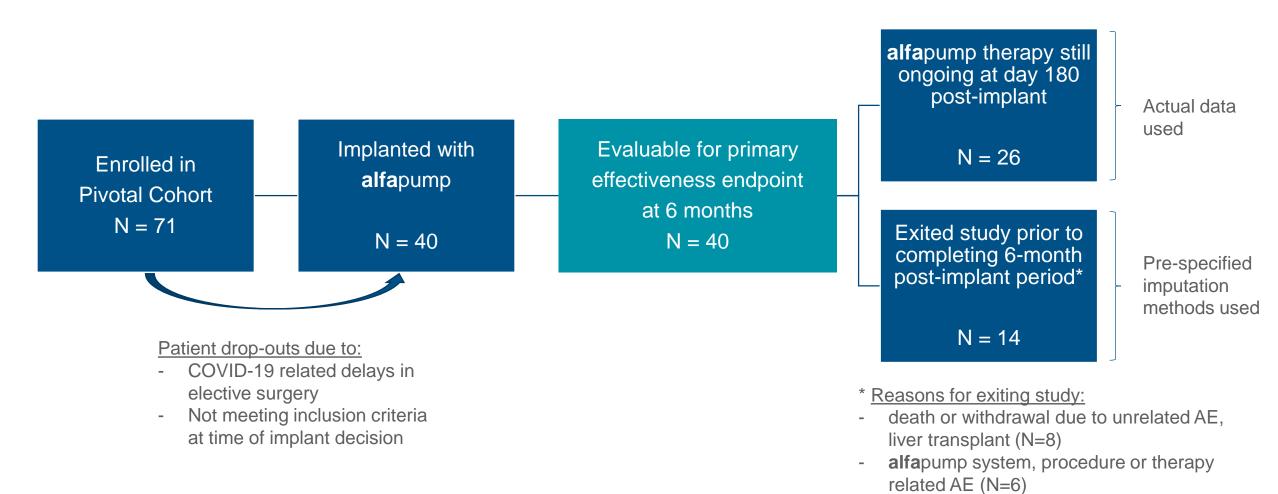
- Outstanding shares: 23.7M
- Outstanding shares corresponding to outstanding share options: 2.7M



- Analysts:
  - Degroof Petercam Laura Roba
  - Edison Pooya Hemami
  - H.C. Wainwright Yi Chen
  - KBC Securities Jeroen Van den Bossche
  - Kempen Suzanne van Voorthuizen
  - Kepler Cheuvreux Arsene Guekam
- Cash (30 June 2022): €23.8M
- Loan facility with Kreos Capital (July 2022): €10M
- Cash runway into Q3 2023

## **POSEIDON – Pivotal cohort**

More than 1/3 of patients implanted with the alfapump® had NASH or combined NASH etiology

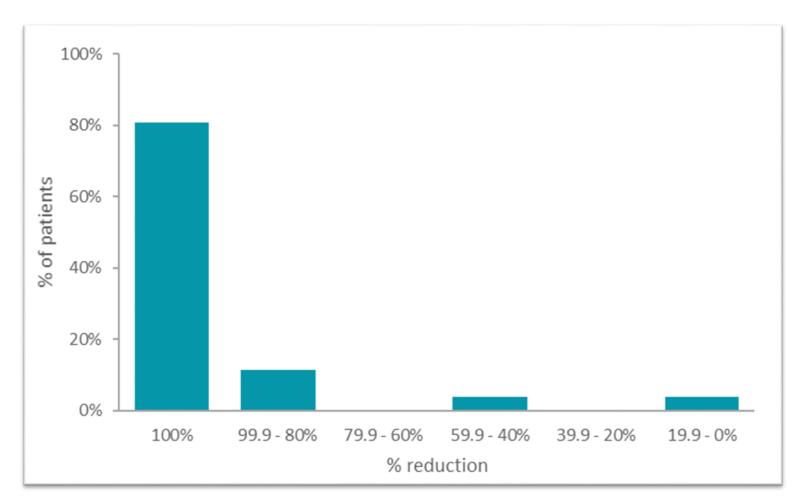




N = 26	%
<ol> <li>Frequency of TP         <ul> <li>a. median per-patient ratio</li> <li>b. mean per-patient ratio</li> </ul> </li> </ol>	100% reduction 93% reduction
2. Proportion of patients with a 50% reduction in number of TP post- vs pre- implantation	92% of patients

## **POSEIDON:** <u>Observed data</u> from patients completing alfapump<sup>®</sup> therapy through day 180 post-implant\*

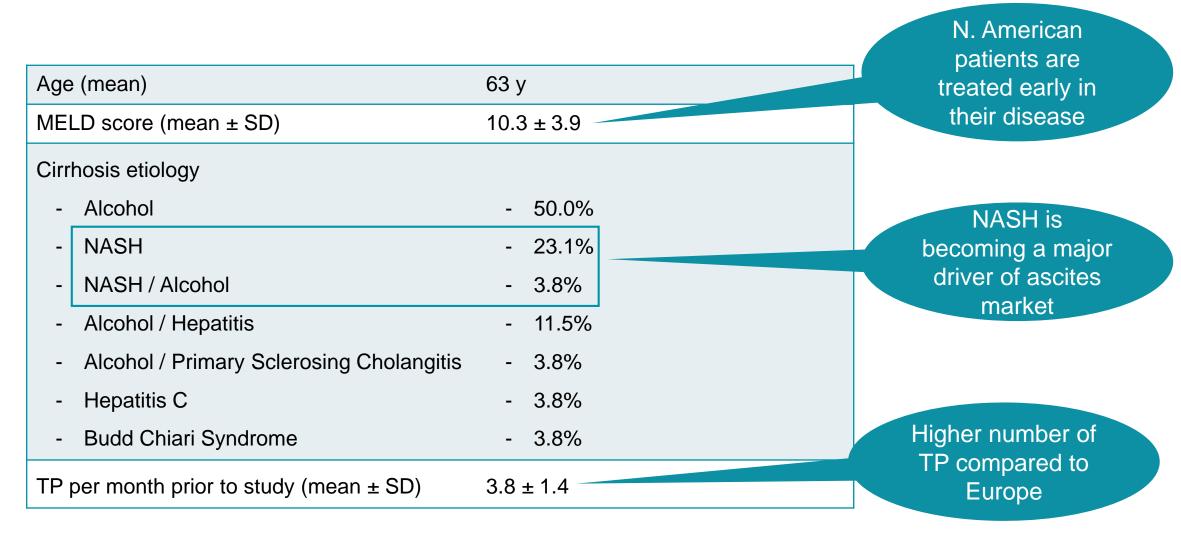
**Distribution of reduction in Therapeutic Paracentesis post-implant vs pre-implant (N = 26)** 



\* These observed patient data are not part of the main primary effectiveness endpoint analysis.

## **Roll-In Cohort: Patient profile**

26 patients with recurrent or refractory ascites



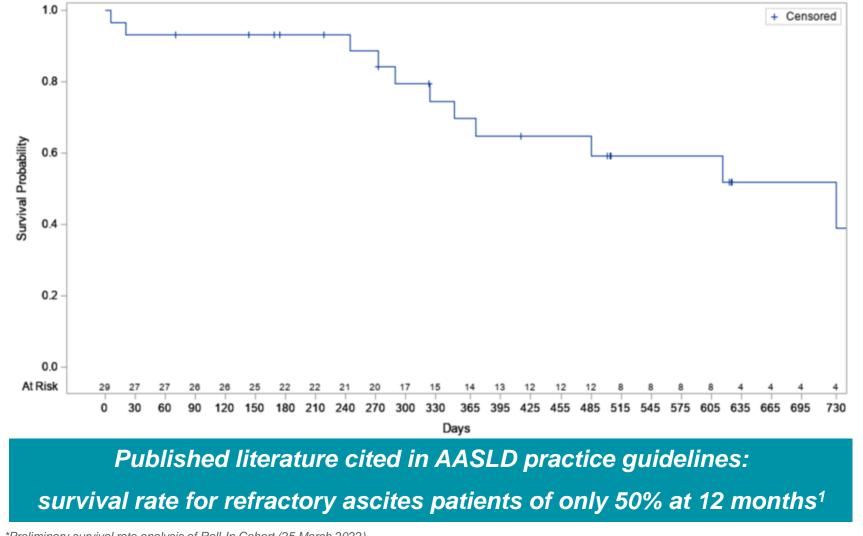
# Roll-In Cohort: Clinically important improvement in quality of life maintained up to 12 months



\* Clinically important improvement: exceeding the threshold for Minimal Clinically Important Difference

## Interim POSEIDON: 70% survival at 12 months\*

Compares favourably to published literature



\*Preliminary survival rate analysis of Roll-In Cohort (25 March 2022)

Source 1: Biggins et al., Hepatology, Vol. 74, No. 2, 2021, AASLD Practice Guidance; Moreau R et al., Liver International 2004: 24: 457-464

## Leading experts as Heart Failure Scientific Advisors



#### Dr. Maria Rosa Costanzo

Medical Director of the Edward Center for Advanced Heart Failure Medical Director Heart Failure Research for the Advocate Heart Institute



#### **Dr. Javed Butler**

Professor and Chairman of the Department of Medicine at the University of Mississippi Medical Center



#### **Dr. Michael Felker**

Professor of Medicine in the Division of Cardiology at Duke University School of Medicine Director of Cardiovascular Research at the Duke Clinical Research Institute and Vice-Chief for Clinical Research in the Division of Cardiology



#### Dr. Wilson Tang

Professor of Medicine at Cleveland Clinic Lerner College of Medicine at Case Western Reserve University



#### Dr. Jeffrey Testani

Associate Professor of Medicine and Director of Heart Failure Research at Yale University School of Medicine

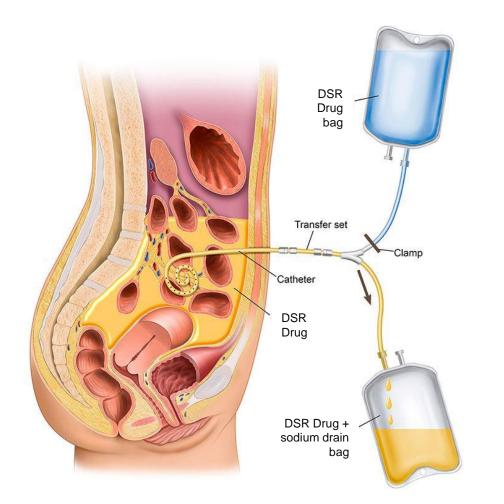


#### Dr. Udelson

Chief of the Division of Cardiology at Tufts Medical Center Professor of Medicine and Radiology at Tufts University School of Medicine

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## **DSR®** therapy treatment overview



Step 1: Peritoneal catheter placement

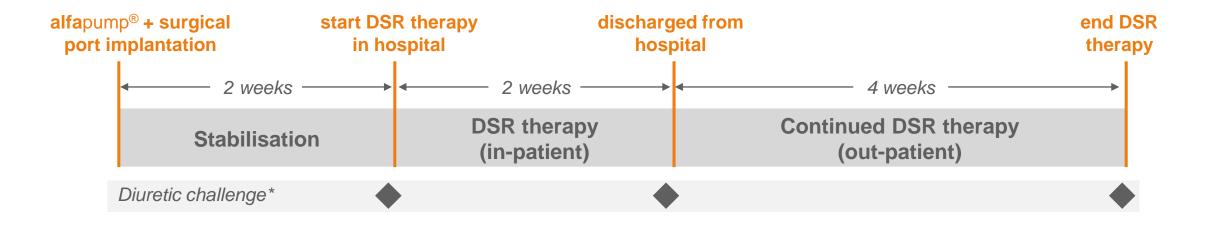
Step 2: DSR treatment episode

- 1. Infusion of DSR Drug
- 2. 24 hour dwell
- 3. Drainage
- Week 1: 5x DSR therapy
- Week 2-4: 3x/week DSR therapy

Step 3: Catheter removal

## **RED DESERT – The first repeated DSR® therapy study**

Repeated dose proof-of-concept study of alfapump DSR® in stable heart failure patients on high dose diuretics



#### **Study Endpoints**

- **Primary:** absence/rate of device, procedure and/or therapy related serious adverse events
- Secondary: ability of the alfapump DSR to maintain a neutral sodium balance in the absence of diuretic therapy and the sustained effect of DSR to maintain euvolemia
- **Exploratory:** impact of DSR to restore response to diuretics following DSR treatment



No loop diuretics required during study despite mean baseline dose of >300 mg/day furosemide equivalents

	Ejection Fraction (%)	NT-proBNP (pg/mL)	Daily Dose of loop diuretics (mg)**	
Subject	At baseline	At baseline	At baseline	During DSR Treatment (D0 - 42)
101-001	26	6,110	80	0
101-002	27	2,863	200	0
101-003	28	1,536	400	0
101-005	25	1,628	120	0
101-006*	23	1,963	80	0
101-007*	26	5,927	300	0
101-008*	20	7,853	600	0
101-009†	20	8,831	800	0
Mean (± SD)	24 ± 3	4,589 ± 2,945	323 ± 263	

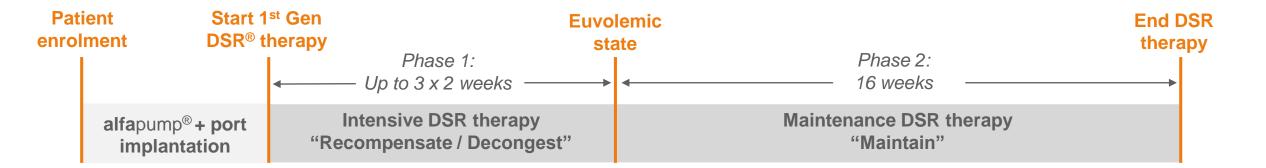
#### Study recruited severely ill heart failure patients on very high doses of oral loop diuretics

\* in follow-up extension with DSR; † subject 101-009 died at D3 \*\* loop diuretics in furosemide equivalents (mg) NT-proBNP: N-terminal-pro hormone B-type Natriuretic Peptide – analysed in local lab

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## **SAHARA: Ph. 2a in target patient population**

Decompensated heart failure patients with persistent congestion on high dose diuretics



#### **Study Endpoints**

- **Primary:** safety and tolerability of **alfa**pump DSR<sup>®</sup> therapy
- **Secondary:** feasibility of DSR therapy to restore and maintain euvolemia without additional loop diuretics

### **SAHARA: Safety**

No clinically relevant changes in serum sodium levels or progressive hyponatremia

- 3 SAEs in 3 patients:
  - Blocked peritoneal catheter (phase 2)

- 2 in 2 patients 🔶
- DMC: related to study device but unrelated to implant procedure or treatment

• Stable angina (extension) – ongoing

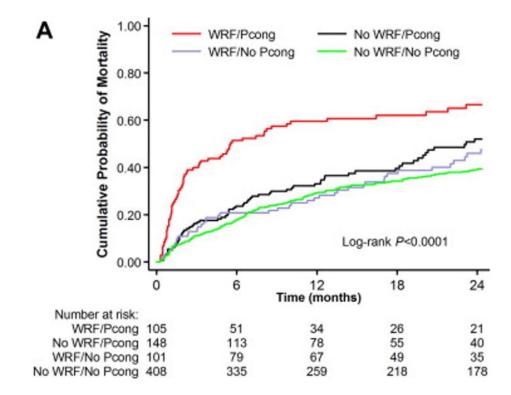
1 in 1 patient

DMC: unrelated to study device, implant procedure or treatment

• No SAEs related to implant procedure or DSR treatment

### **Persistent congestion and Worsening renal function**

Persistent congestion and worsening renal function are key targets in decompensated heart failure



Wattad et al, American Journal of Cardiology, 2015: interaction between worsening renal function and persistent congestion in acute decompensated heart failure (study of 762 patients)

## **Evaluating potential for DSR® in renal failure**

Complementary opportunity leveraging heart failure programme capabilities

- Like heart failure, kidney failure / dialysis is one of the leading burdens for healthcare systems and carries a high mortality / morbidity burden
- Hemodialysis seeks to tackle two different challenges removal of uremic toxins as well as managing the sodium and fluid balance – creating clinical and economic challenges
- DSR therapy has the potential to more effectively manage the fluid and sodium balance of this large patient group
  - ⇒ Leveraging all of our experience from congestion / fluid overload in heart failure
- We are exploring the potential of DSR in this large and important patient group, potentially reducing hospitalisations, the cost and burden of hemodialysis therapy as well as mortality
  - Supporting work of Dr McIntyre (Lawson Health Research Institute, Ontario, Canada): evaluating the use of DSR therapy in effective volume management and sodium removal in prevalent hemodialysis patients (NCT04603014)