

sequana**medical**



Innovators in the treatment of
diuretic-resistant fluid overload
liver disease – malignant ascites – heart failure

Investor presentation – May 2021

Disclaimers

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Disclaimers

Regulatory disclaimer:

- The **alfapump**[®] 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**[®] system does not apply to the United States and Canada. In the United States and Canada, the **alfapump**[®] 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 www.poseidonstudy.com.
- DSR[®] 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[®] therapy is currently not approved for clinical research in the United States or Canada. There is no link between DSR[®] therapy and ongoing investigations with the **alfapump**[®] 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**[®] is a registered trademark. DSR[®] and **alfapump DSR**[®] are registered trademarks in Benelux.

Sequana Medical NV

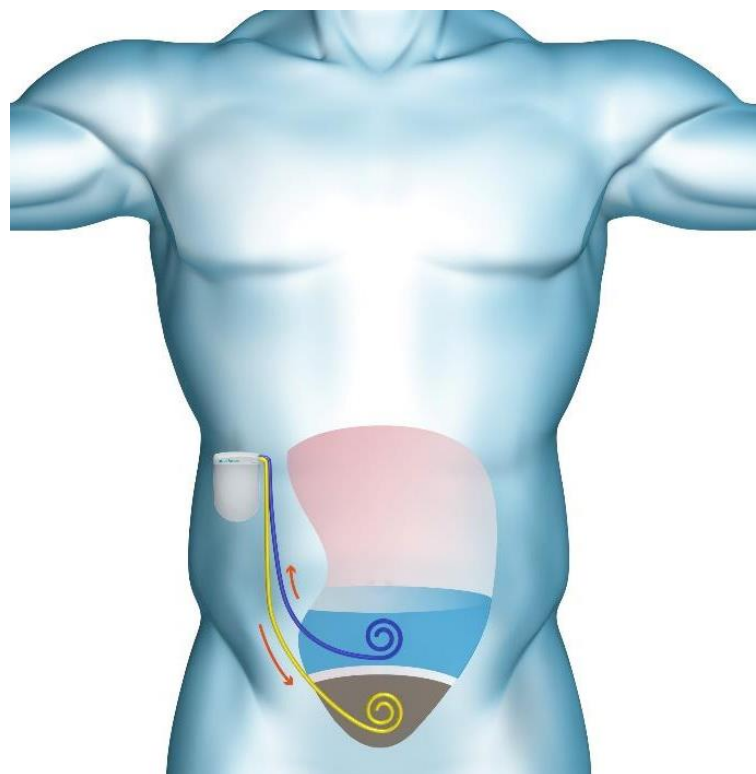
- Founded in 2006
- Gent, Belgium (HQ): corporate, clinical, commercial
- Zurich, Switzerland: manufacturing, engineering, QA/RA
- ~50 employees
- Euronext Brussels: SEQUA



alfapump[®] platform

Using the bladder to treat fluid overload

- ✓ Fully implanted
- ✓ Automatic operation
- ✓ Wireless battery charging
- ✓ Settings wirelessly adjusted
- ✓ Remote data monitoring



- ✓ Easy implantation
- ✓ Long-term implantation & catheter patency
- ✓ Moves up to 4 litres / day
- ✓ Virtually non-clogging
- ✓ No significant heating during charging and operation

Strong IP barriers through extensive patent portfolio & know-how

One platform – two products – € billion opportunities



alfapump®

Liver Disease (NASH)

Proven step change in liver refractory ascites and malignant ascites

Over 850 devices implanted

> €3 Bn / year market opportunity⁽¹⁾



POSEIDON pivotal study ongoing

Self-commercialisation



alfapump DSR®

Heart Failure

Breakthrough approach to fluid overload in heart failure

Clinical proof-of-concept of Direct Sodium Removal (DSR®)

> €5 Bn / year market opportunity⁽²⁾



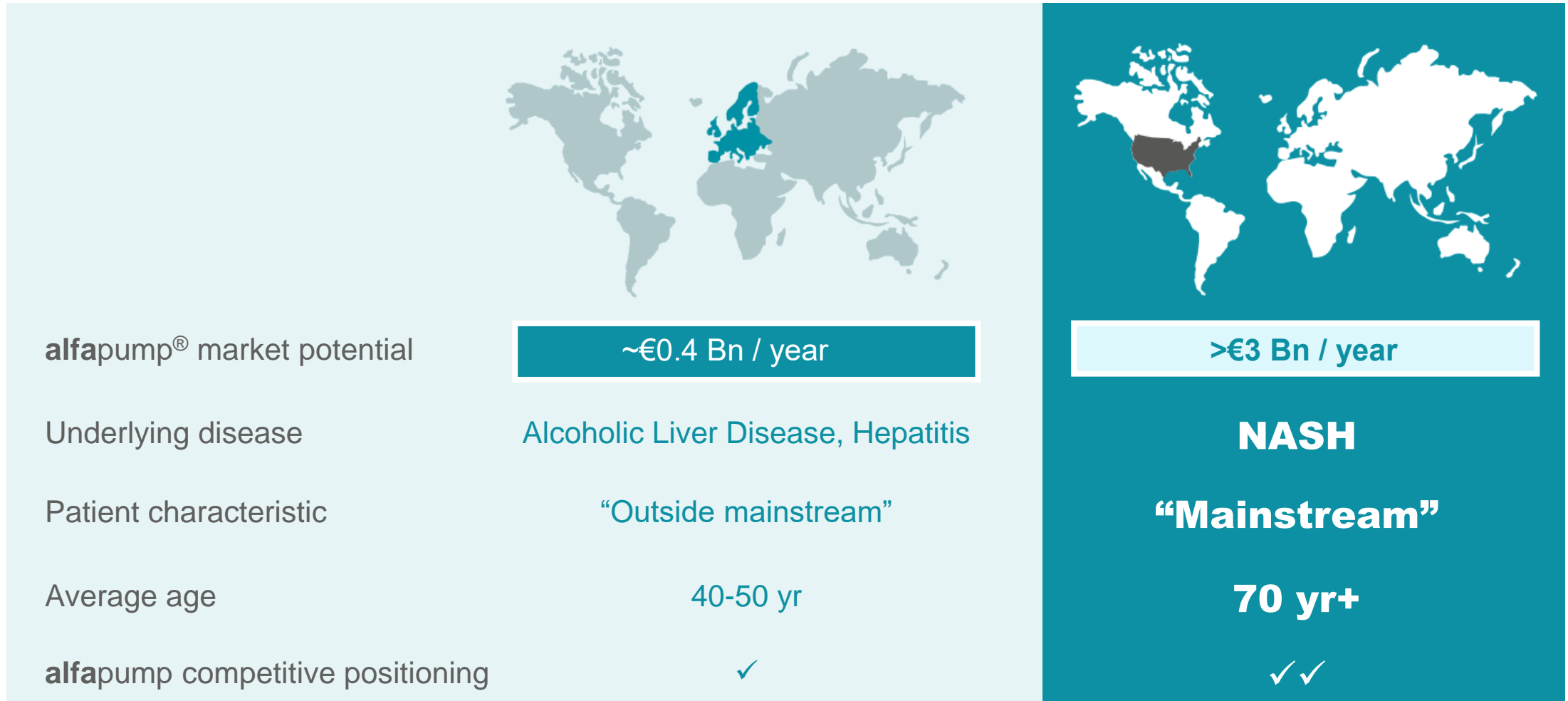
RED DESERT repeated dose study ongoing

Partnering after US efficacy study

Built upon proven European clinical & commercial experience

NASH drives US market attractiveness

Stronger competitive position in a much larger and dynamic market



Notes: current estimated EU Liver market: Data from 1980-2010, death rates between 9-12.4 per 100,000; Mokdad et al., 2014, Management estimates of 7.5% cirrhosis patients that die per year based on experts feedback. forecast US Liver market: Management estimate that is inclusive of estimated growth in prevalence of NASH for the US based on GlobalData Epidemiology Forecast to 2026.



alfapump®

Proven step change in the management of liver refractory ascites and malignant ascites

Liver cirrhosis and refractory ascites

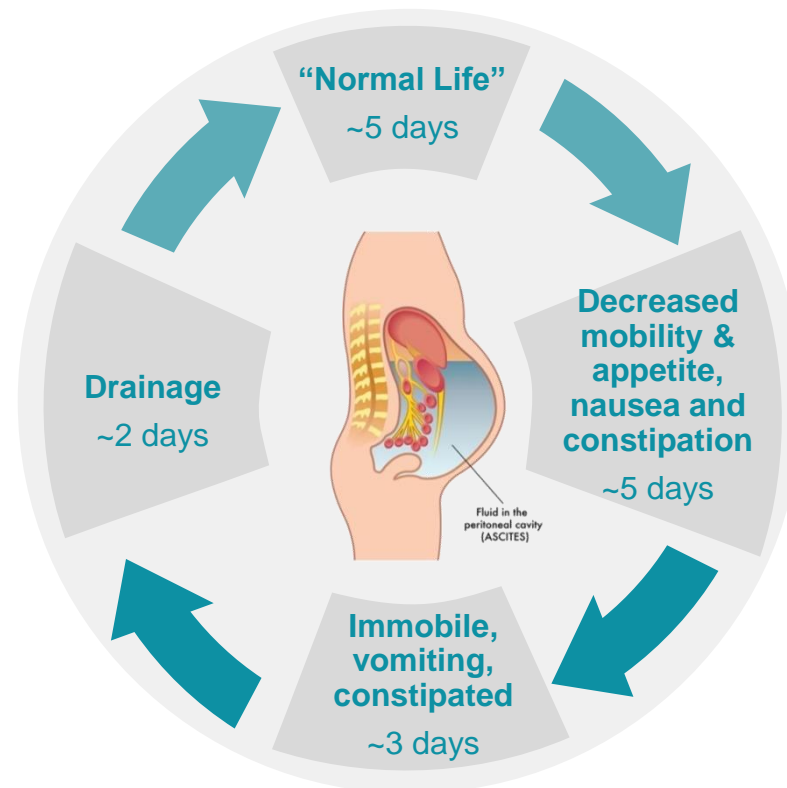
A key complication of liver cirrhosis, with a dramatic impact on quality of life

- 

Viral infections
(Hepatitis B & C)
- 


Alcoholic Liver Disease
- 

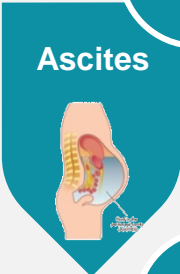
Non-Alcoholic Steatohepatitis (NASH)




Typical patient life⁽⁴⁾

US forecast

- 

Liver cirrhosis
~3-4M⁽¹⁾
- 

Ascites
~1.5M⁽²⁾
- 

Refractory Ascites
~150K⁽³⁾

Note : Prevalence of NASH in US is expected to increase by 63% between 2015-2030; Estes et al., 2018

Source 1 Management estimate in US based on Estes et al; GlobalData Nash Epidemiology Forecast to 2026; Noureddin et al., 2013

Source 2: Runyon 2009: approximately 50% of cirrhotic patients develop ascites within 10 years of diagnosis of cirrhosis

Source 3: Ginès et al., NEJM 2004: refractory ascites occurs in 5-10% patients with ascites

Source 4: Presentation of Dr. Rajiv Jalan at EASL in 2018, Large Volume Paracentesis (LVP) treatment cycle for refractory ascites

Cancer and malignant ascites

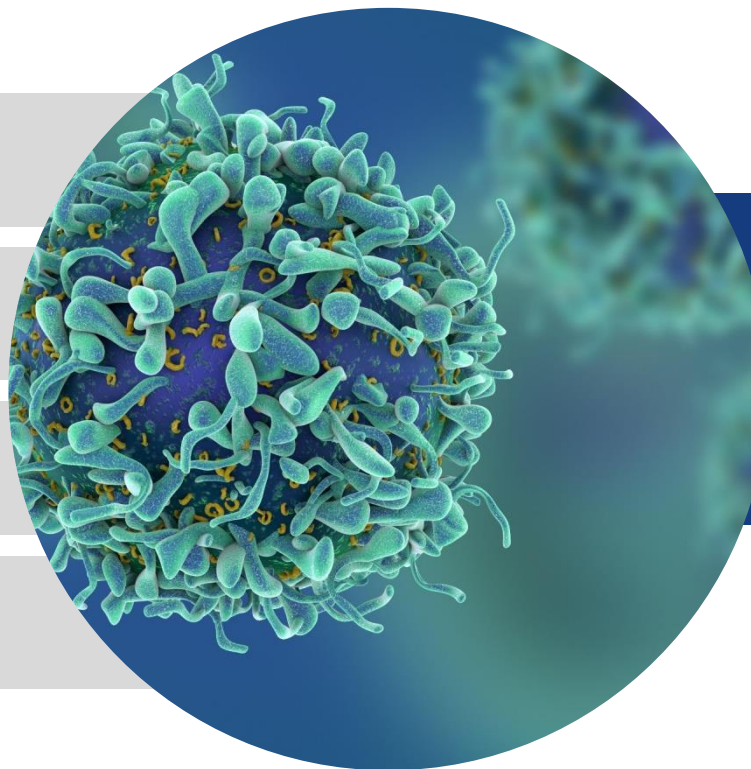
Severe complication of late-stage cancers

Fluid accumulation in the abdomen due to **drainage of lymph system**

Breast and ovarian cancer have longest survival with ascites⁽¹⁾

Severe impact on **quality of life**

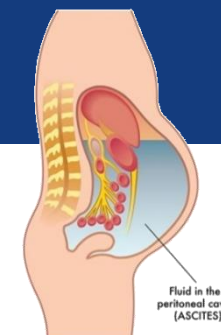
Reduces ability to undergo **anti-cancer treatment**



Malignant ascites due to breast and ovarian cancer⁽²⁾:

EU5: ~18K

US: ~16K



Clear unmet need for improving Quality of Life and the ability to increase cancer treatment intensity

Source 1: Ayantunde & S. L. Parsons. Annals of Oncology 2007

Source 2: Management estimate based on WHO cancer incidence rates (2018) and Ayantunde & S. L. Parsons. Annals of Oncology 2007.

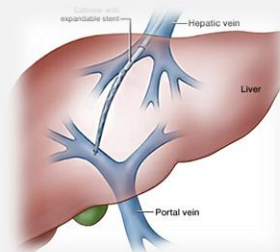
Severe limitations of existing therapies

Diet / Diuretics



Resistance,
Complications

Transjugular Intrahepatic Portosystemic Shunt (TIPS)



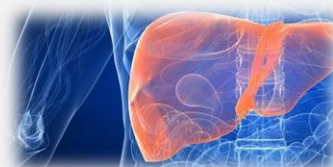
Complications,
Contraindications

Drainage (“Large Volume Paracentesis / LVP”)



Painful, Poor Quality of
Life, Short Term Benefit

Liver transplantation



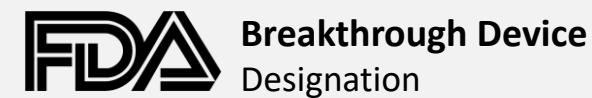
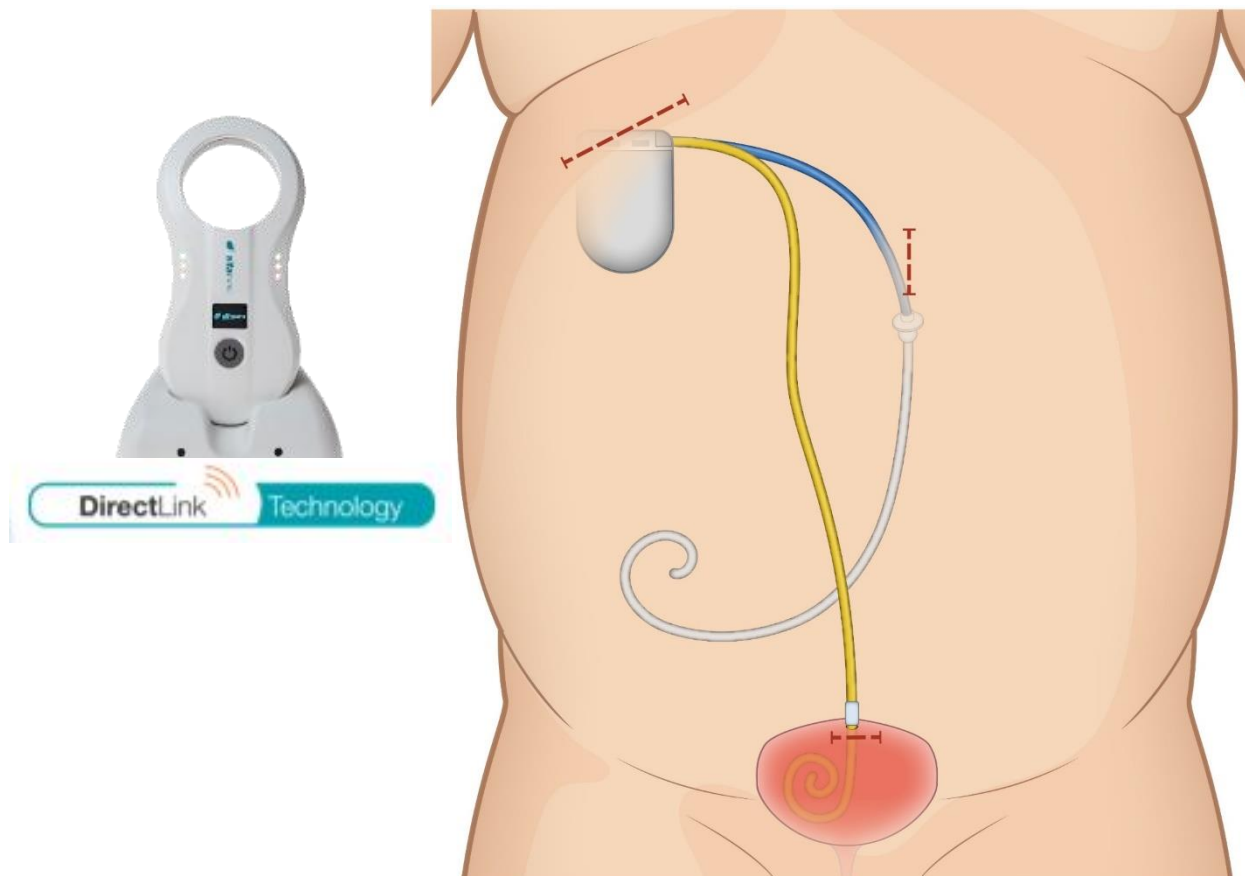
High Cost,
Limited Availability

alfapump®






alfapump® for long-term treatment

Over 850 implants and hundreds of years of patient experience



Strong clinical and economic rationale

-  Reduced burden of disease
-  Improved patient QoL
-  Cost savings for hospitals and payers

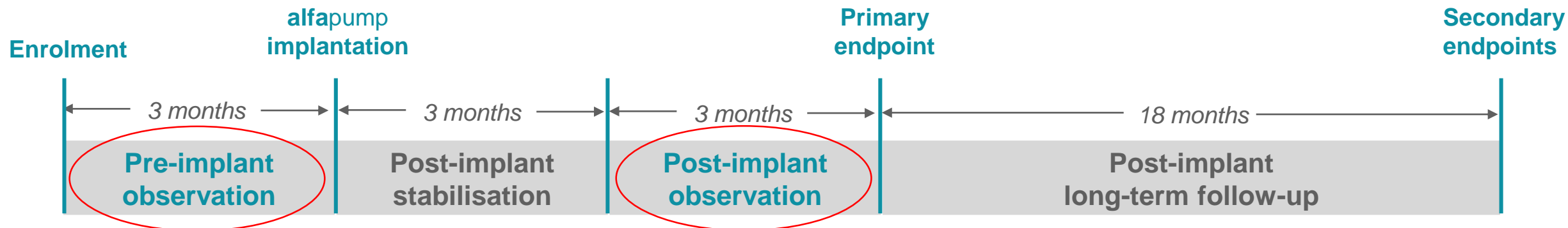
Estimated treatment cost / patient*:

LVP: ~\$54K		alfapump®: ~\$35K
~\$1,8K / LVP ⁽¹⁾		~\$25K / alfapump
2 LVP / month		~\$10K / implantation
15 months		

* Management estimate of US treatment costs, assuming no complications

North American Pivotal Study (POSEIDON) underway

Pivotal Cohort of up to 50 patients implanted; Roll-In (“training”) cohort of up to 30 patients



POSEIDON Study Endpoints

Primary efficacy: 1) 50% reduction in average monthly frequency of Therapeutic Paracentesis (“TP”) post-implant vs. pre-implant
2) 50% of patients achieve a 50% reduction in the requirement for TP post-implant vs. pre-implant

Primary safety: Rate of **alfapump** related re-interventions adjudicated by the Clinical Events Committee (CEC)

Secondary: QoL (SF36, Ascites-Q), nutritional status, health economics, safety (device and/or procedure-related AEs), survival

POSEIDON Interim Data: Positive for primary endpoints

Data from first 13 Roll-In patients

EFFICACY

Mean values post-implant vs. pre-implant	N = 13
Reduction in frequency of TP	> 90%
Patients with >50% reduction in TP	100%

SAFETY

- Safety profile of the **alfapump** consistent with previously reported data
- Adjudication process by the Clinical Events Committee for two **alfapump**[®] explants ongoing

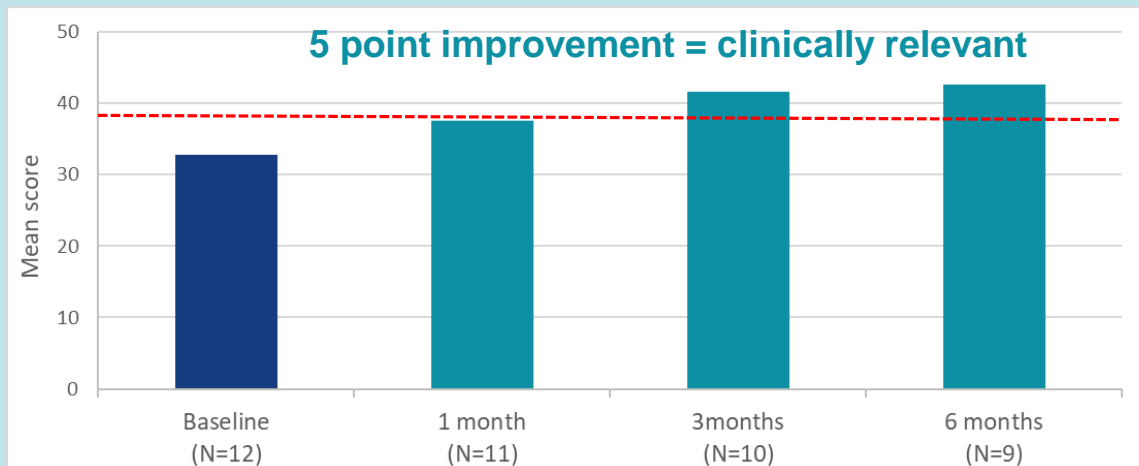
Note: Pre- and post-implant periods for this analysis of the Roll-In Cohort differ from those that will be used for the Pivotal Cohort analysis

Quality of Life: Indication of fast and persistent improvement

SF-36

General health-survey questionnaire

Physical Component Score



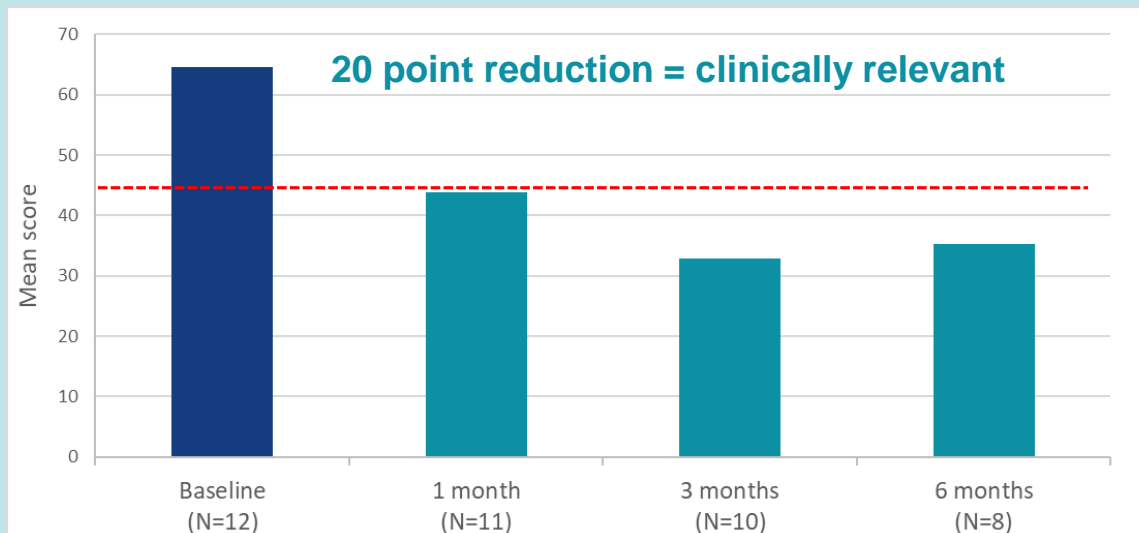
Higher is better



Ascites Q

Specific health-survey questionnaire for ascites

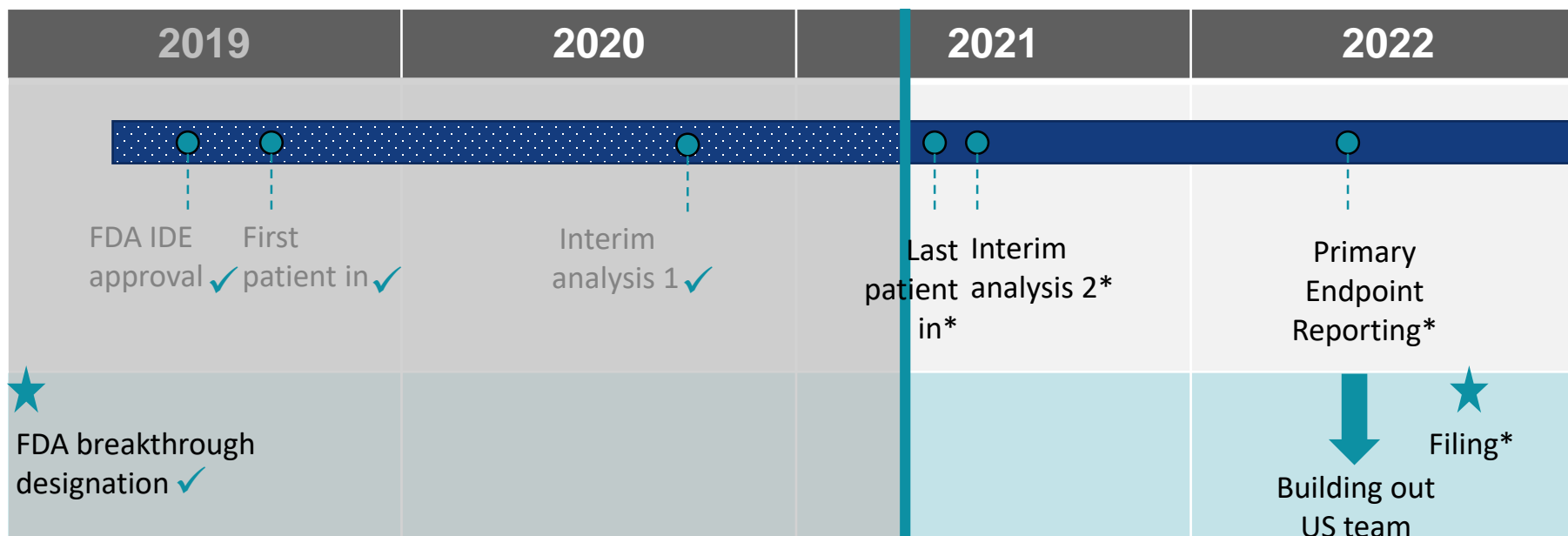
Total Score



Lower is better



Targeting announcement of primary endpoint in Q2 2022

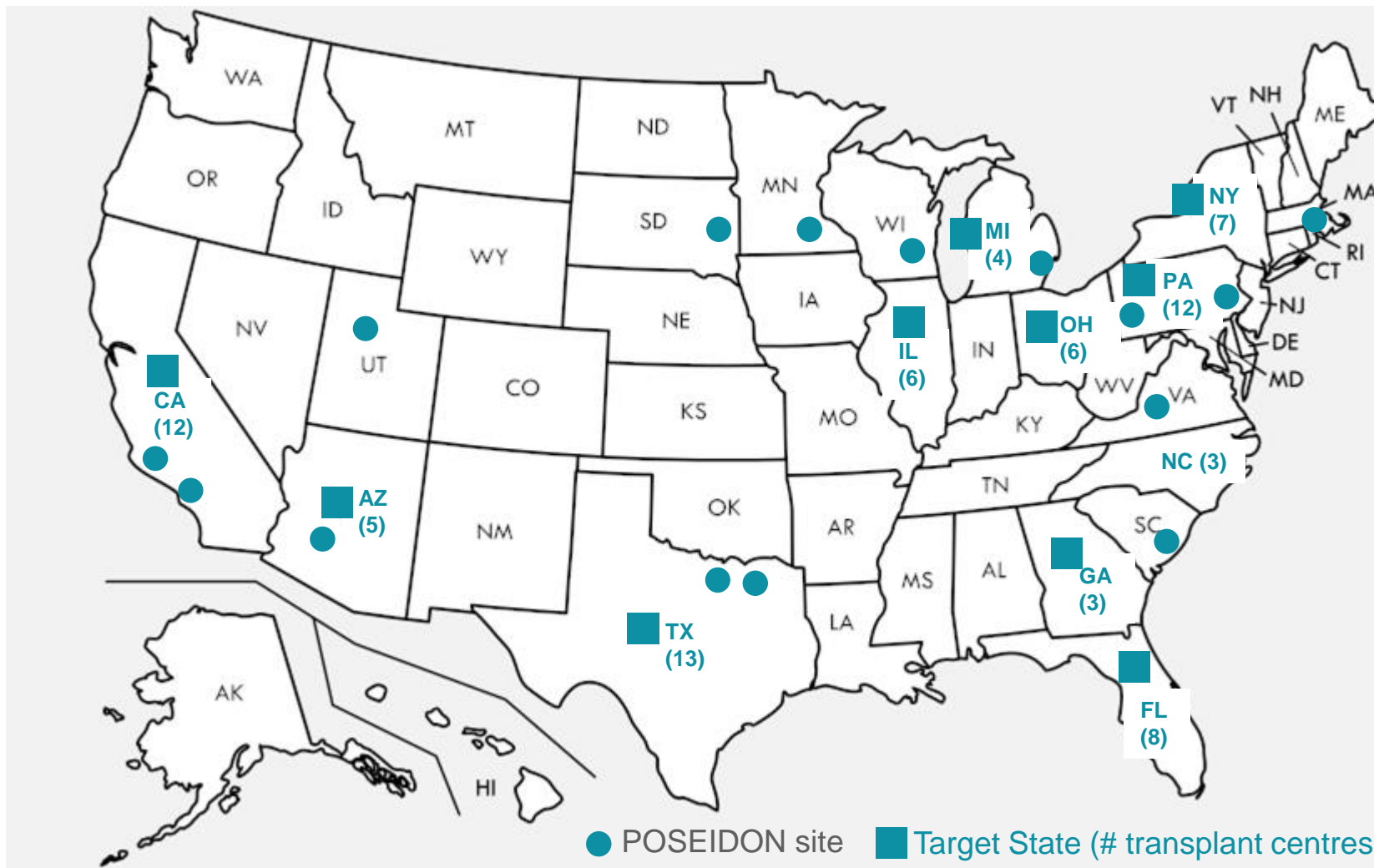


*MCIT & NTAP – CMS initiatives for breakthrough devices to further support coverage & reimbursement for the **alfapump***

* Subject to further developments related to the ongoing COVID-19 pandemic

FDA: Food and Drug Administration (US); IDE: Investigational Device Exemption

US commercialisation through our specialty salesforce



Initial focus on key transplant centres

~50-person team:
35 sales reps, 10 clinical,
5 corporate

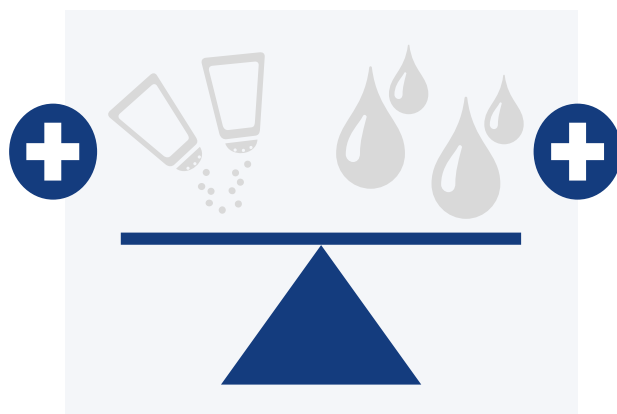


alfapump DSR[®]

Breakthrough approach to **fluid overload in heart failure** built on proven **alfapump[®]** platform

Diuretic-resistant fluid overload in heart failure

Key clinical challenge and driver of costs



Excess sodium drives
fluid overload

US hospitalisations
annually due to
HF⁽³⁾

~1m

90%

HF –
hospitalisations
due to fluid
overload⁽³⁾



c.5d

Typical
hospital stay⁽⁴⁾

Annual costs of US
HF-related
hospitalisations⁽⁴⁾

\$13bn

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

Direct Sodium Removal (DSR®)

Proprietary approach to fluid overload – supported by interim RED DESERT clinical data

We remove the sodium and then the body “does the math” to maintain serum sodium balance



“DSR represents a new potential therapy for non-renal sodium and fluid removal in edematous disorders such as heart failure”

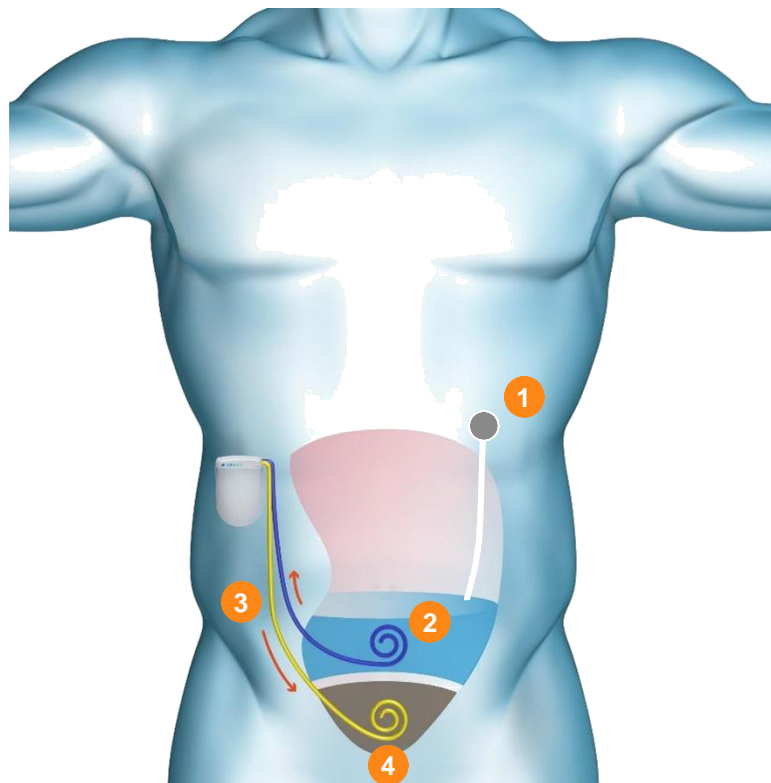
Circulation First in Human Experience with Peritoneal Direct Sodium Removal Using a Zero Sodium Solution: A New Candidate Therapy for Volume Overload

Veena S. Rao, Jeffrey M. Turner, Matthew Griffin, Devin Mahoney, Jennifer Asher, Sangchoon Jeon, Peter S. Yoo, Nabil Boutagy, Attila Feher, Albert Sinusas, F. Perry Wilson, ... [Show all Authors](#) ▾

Originally published 8 Jan 2020 | <https://doi.org/10.1161/CIRCULATIONAHA.119.043062> | Circulation .0.null

alfapump DSR[®]

Potential chronic therapy for diuretic-resistant heart failure patients with fluid overload

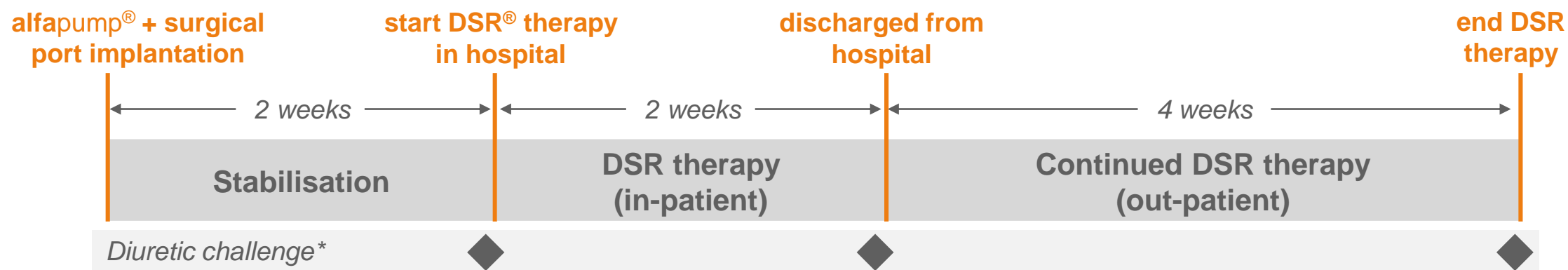


- 1 Sodium-free DSR[®] infusate administered to peritoneal cavity via implanted port
- 2 Sodium diffuses into DSR infusate
- 3 **alfapump** pumps sodium-rich DSR infusate into the bladder
- 4 Body eliminates excess fluid through osmotic ultrafiltration and urination

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

RED DESERT: Study design

Repeated dose proof-of-concept study of alfapump DSR® in diuretic-resistant heart failure patients



✓ **Positive interim results (5 patients) reported**

Top-line results (up to 10 patients) expected in Q2 2021

*40mg IV furosemide to evaluate diuretic response (6 hour sodium and fluid excretion)

Interim RED DESERT: Strong safety & efficacy results

Results from first five patients

SAFETY

- Implant procedure of **alfapump DSR[®]** and repeated dosing of DSR[®] therapy were **well-tolerated**
- No clinically significant changes in serum sodium levels / **no progressive hyponatremia**
- Reported **adverse events were manageable**

EFFICACY

- **No diuretics required** in any of the patients during 6-week **alfapump DSR** treatment
- Reduced doses of DSR therapy and / or less frequent DSR dosing in majority of patients
⇒ maintaining stable to lower weight and NT-proBNP compared to baseline

Interim RED DESERT: Restored normal kidney response

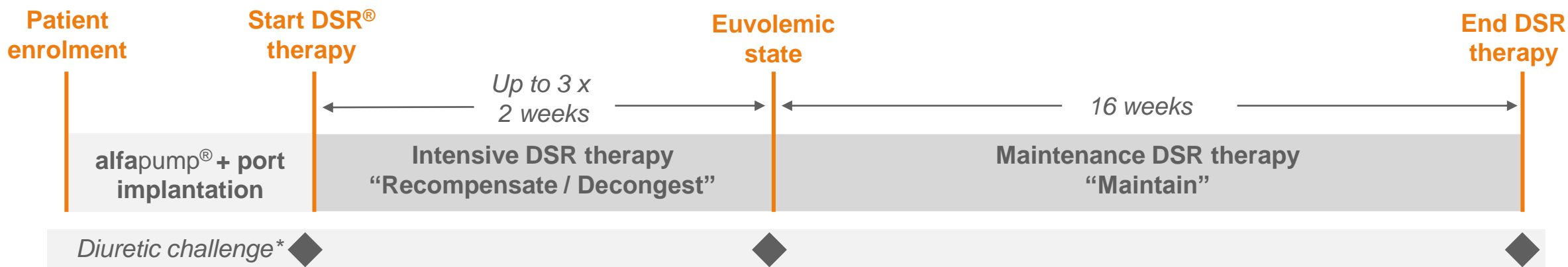
Results from first five patients

- **Diuretic response restored to near normal levels**
 - Sodium excretion more than doubled after DSR study period (to near normal levels)
- **Long-lasting improvement in diuretic responsiveness**
 - Dramatic reduction in oral loop diuretic dosage in majority of patients at end of DSR study period
 - Major reduction in oral diuretic dosage vs baseline even months after end of DSR study period

- *Indicates DSR therapy is more than just a means to remove sodium and water*
- *Supports intermittent dosing to restore natural kidney response*
- *Potential expansion into other fluid overload indications*

SAHARA DESERT – decongestion & diuretic response

20 decompensated heart failure patients with residual congestion on high doses of loop diuretics



Study Endpoints

- **Primary:** safety and tolerability of **alfapump DSR®** therapy
- **Secondary:** feasibility of DSR therapy to restore and maintain euvoemia without additional loop diuretics
- **Exploratory:** evaluate potential impact of SGLT-2 inhibitors on DSR therapy**

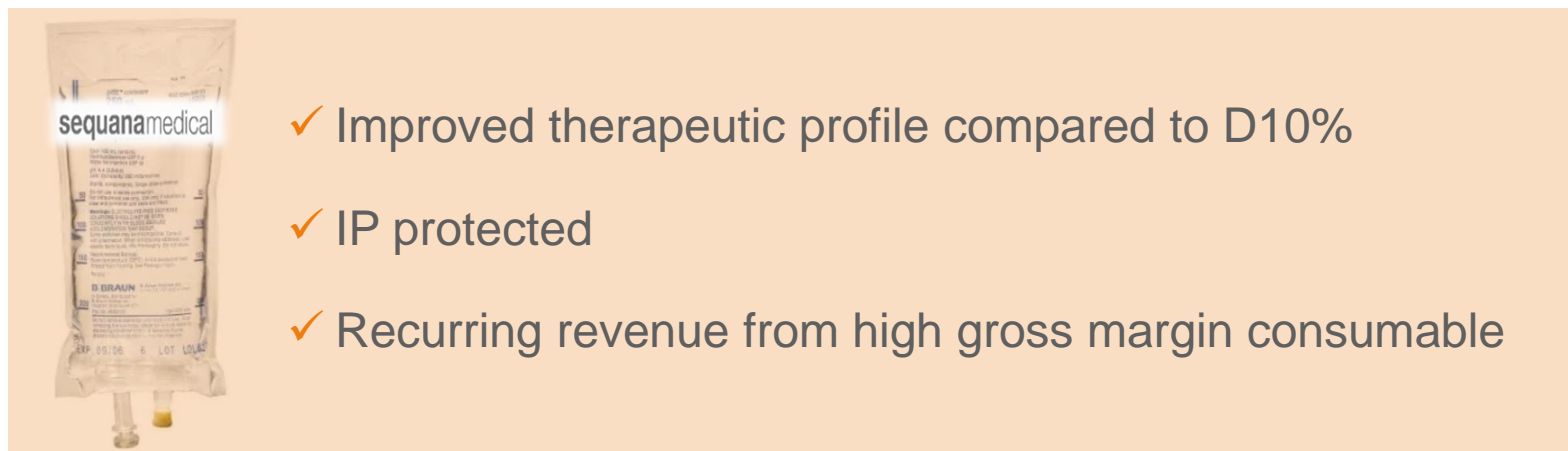
Anticipated Timing: Start Q2 2021 / Interim results Q4 2021 / Top-line results H1 2022

* 40mg IV furosemide to evaluate diuretic response (6 hour sodium and fluid excretion)

** patients will be randomised 1:1 to DSR therapy +/- SGLT-2 inhibitor therapy

Developing high value proprietary DSR[®] Infusate

- D10% was chosen as the initial DSR infusate for fastest proof-of-concept
- We are developing our **proprietary next-generation DSR infusate**:



Note: This image is intended for illustration purposes only

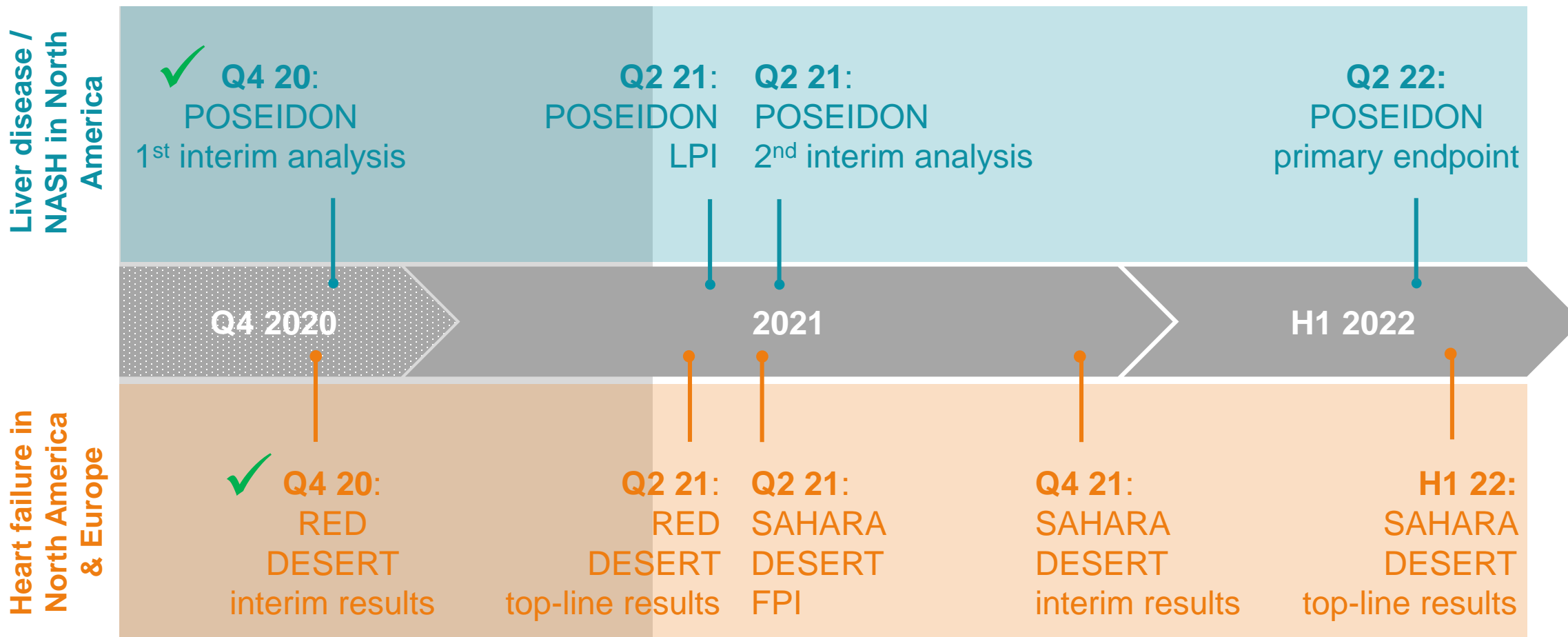


Outlook

Strong **near term value drivers**
with clear **long term potential**



Expected core value drivers & outlook



Note: Presented timelines are subject to further developments related to the COVID-19 pandemic

Back-up



Strong organisation

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

Executive team:



Ian Crosbie
Chief Executive Officer



Kirsten Van Bockstaele
Chief Financial Officer



Oliver Gødje
Chief Medical Officer



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



Ian Crosbie
Chief Executive Officer



Wim Ottevaere
Director



Jason Hannon
Director



Rudy Dekeyser
Director

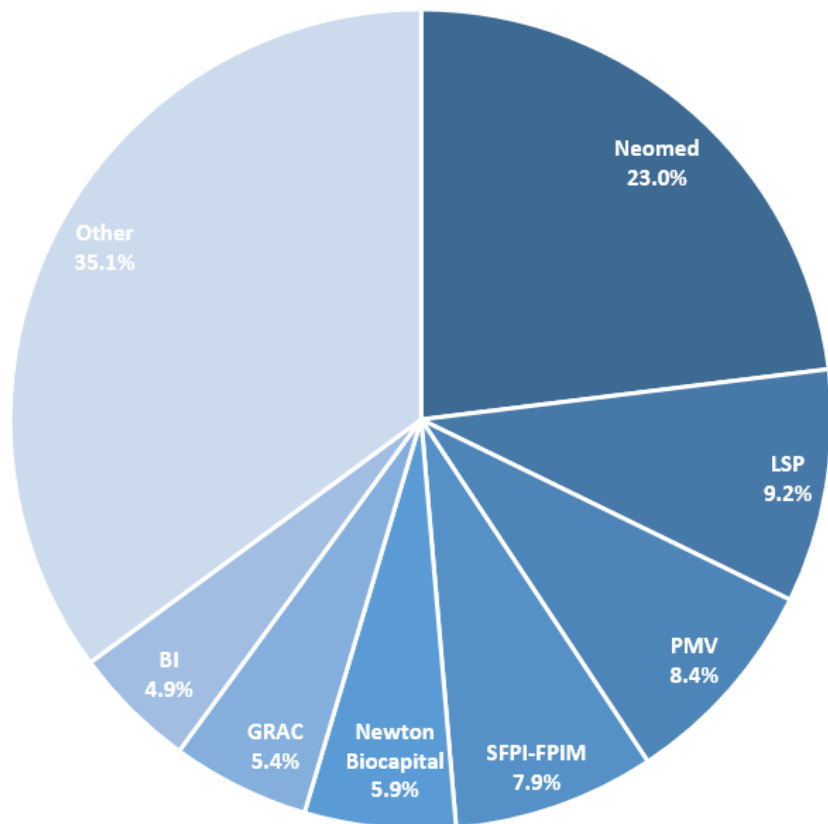


Erik Amble
Director

Shareholders base and financial overview

Ticker: SEQUA – Euronext Brussels

- Outstanding shares: 18.5M
- Outstanding share options & warrants: 1.8M



- Analysts:
 - KBC Securities – Lenny Van Steenhuyse
 - Kempen – Ingrid Gafanhão
 - Kepler Cheuvreux – Matthias Maenhaut
 - Mirabaud – Daniel Jelovcan
- Cash (31 December 2020): €11.0M
- Equity financing in February 2021: €22.5M
- Cash runway into Q2 2022



POSEIDON – study cohorts

Patients with recurrent or refractory ascites due to liver cirrhosis in up to 20 centres across US and Canada

Two study cohorts with the same inclusion / exclusion criteria

1 Pivotal Cohort

- Up to 50 patients implanted with the **alfapump**[®]
- For primary and secondary endpoint analysis

2 Roll-In Cohort ➡ enables us to report interim data

- Up to 30 patients implanted with the **alfapump**
- To teach clinicians and medical teams at new centres how to use the **alfapump**



Cirrhotic patients with recurrent or refractory ascites

First 13 patients in Roll-In Cohort of the POSEIDON study

Age (mean)	65 y
MELD score (mean ± SD)	10.5 ± 4.6
Cirrhosis etiology	
- Alcohol	- 61.5%
- NASH	- 23.1%
- Hepatitis C	- 7.7%
- Alcohol, Hepatitis C, and Hepatitis B	- 7.7%
TP per month prior to study (mean ± SD)	3.4 ± 1.8

Willingness to treat earlier stage patients?

NASH is already an important driver of this market

N. American patients appear to have more TP / month compared to Europe

MELD: Model for End-stage Liver Disease; SD: Standard Deviation; NASH: Non-Alcoholic Steatohepatitis; TP: Therapeutic Paracentesis



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. Wilson Tang

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



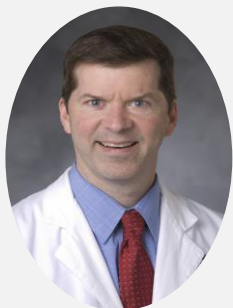
Dr. Javed Butler

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



Dr. Jeffrey Testani

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



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. Udelson

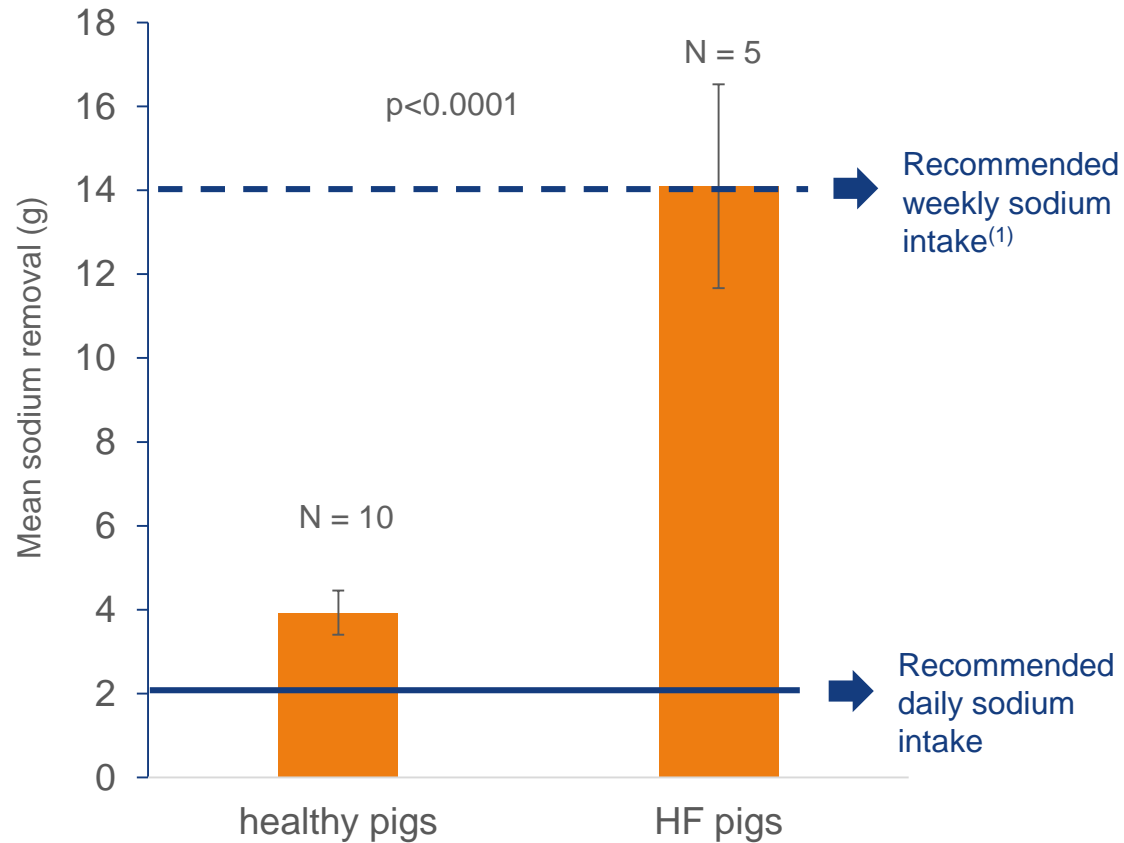
Chief of the Division of Cardiology at Tufts Medical Center
Professor of Medicine and Radiology at Tufts University School of Medicine



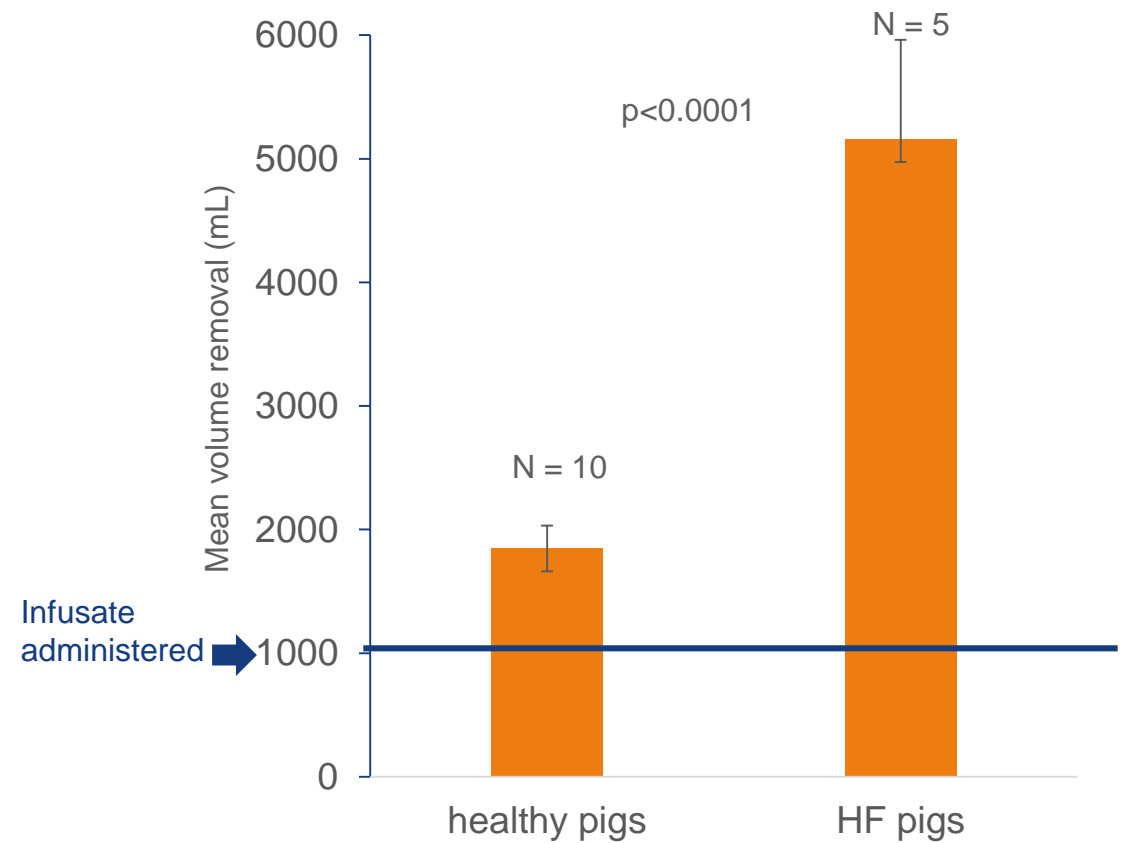
DSR[®] pre-clinical Proof-of-Concept

Clinically relevant sodium and fluid removal

Clinically relevant removal of sodium



Effective fluid removal

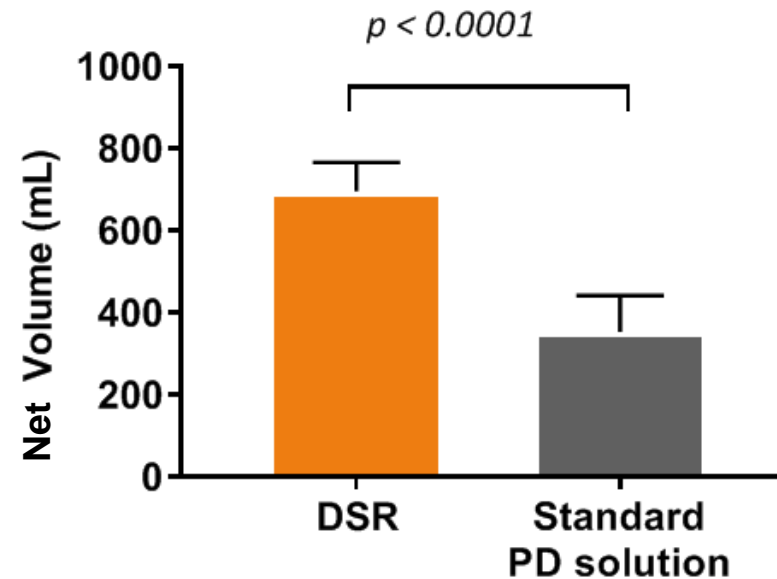
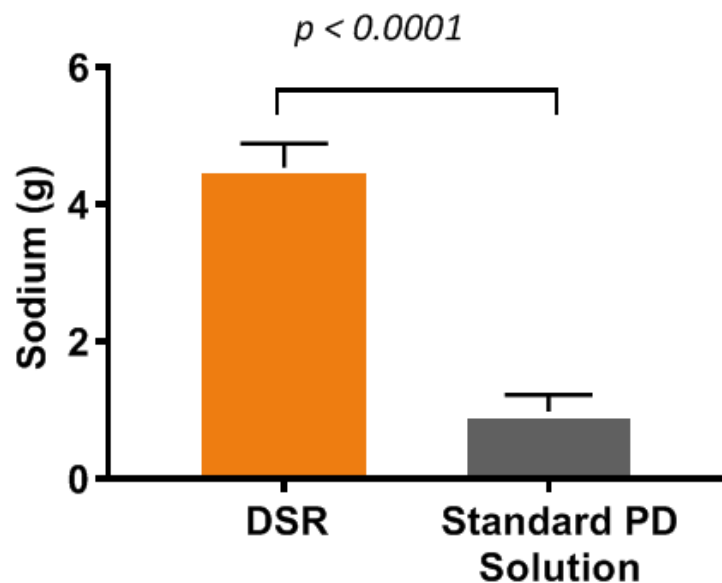


Source 1: Weekly recommended intake for humans equals 14 grams (www.cdc.gov)



DSR[®] first-in-human study met primary and secondary endpoints

- ✓ DSR therapy was safe & well-tolerated with no adverse events or significant discomfort
- ✓ Substantially higher sodium removal with DSR vs standard Peritoneal Dialysis (PD) solution
- ✓ Minimal inter-patient variability



*Results presented at
key Cardiac
Conferences and
published in
Circulation*

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