



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

Investor presentation – January 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 see www.poseidonstudy.com.
- The DSR therapy is still in development and it should be noted that any statements regarding safety and efficacy arise from ongoing pre-clinical and clinical investigations which have yet to be completed. The DSR therapy is not currently approved for clinical research in the United States or Canada. There is no link between the DSR therapy and ongoing investigations with the **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 its operations as necessary.
- Sequana Medical has put in place mitigation plans to minimise delays. The impact of increased demands on the healthcare systems, restrictions 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.

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



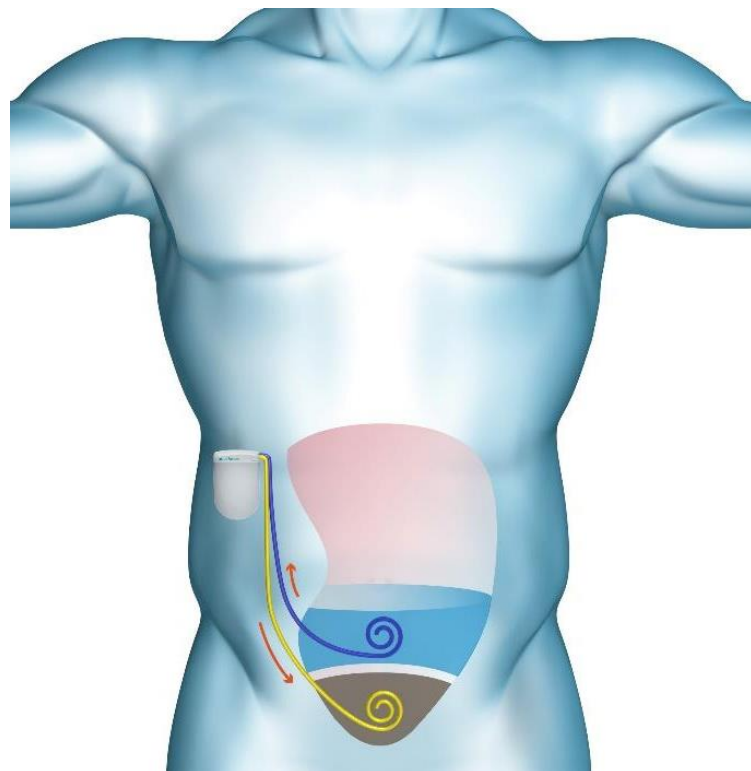
Wireless battery charging



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



alfapump®

Liver Disease (NASH)

Proven step change in liver refractory ascites
and malignant ascites

Over 800 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⁾



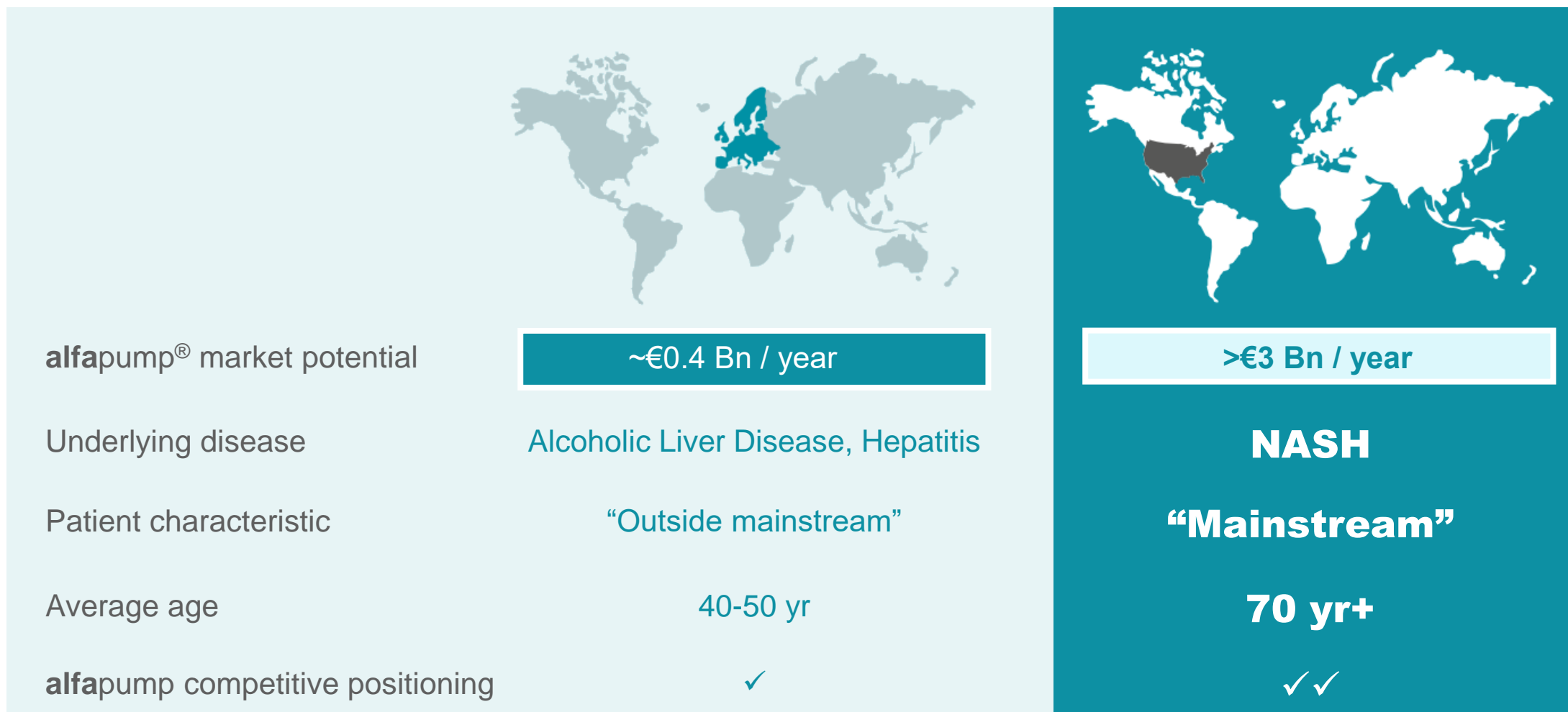
RED DESERT repeated dose study ongoing

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





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

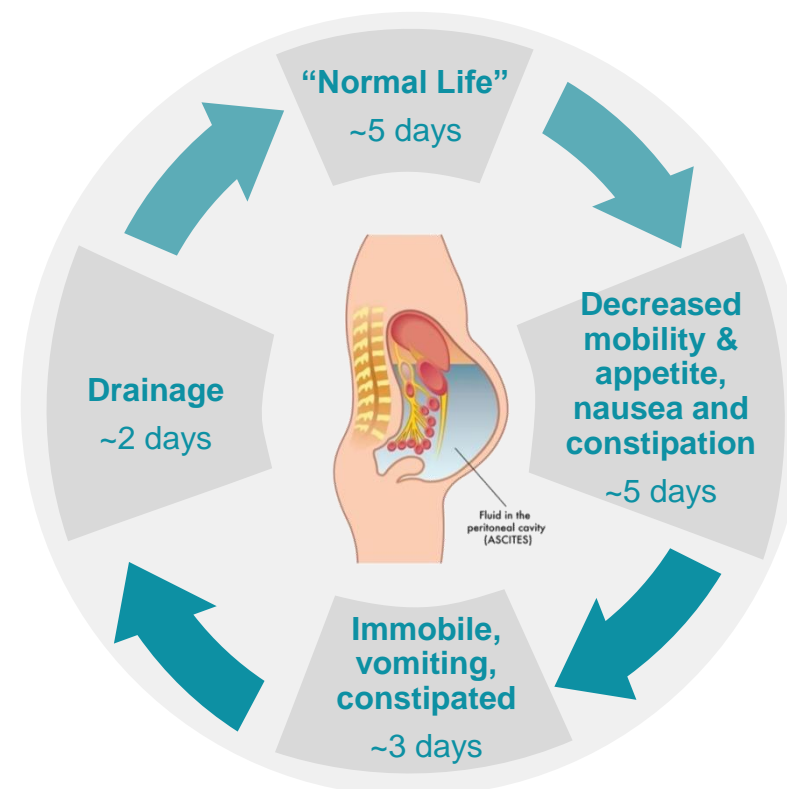
Viral infections
(Hepatitis B & C)



Alcoholic Liver Disease



Non-Alcoholic Steatohepatitis (NASH)



Typical patient life⁽⁴⁾

US forecast

~3-4M
(1)

Liver cirrhosis



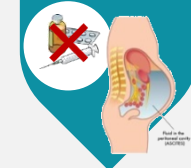
~1.5M
(2)

Ascites



~150K
(3)

Refractory Ascites



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; Nouredin 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

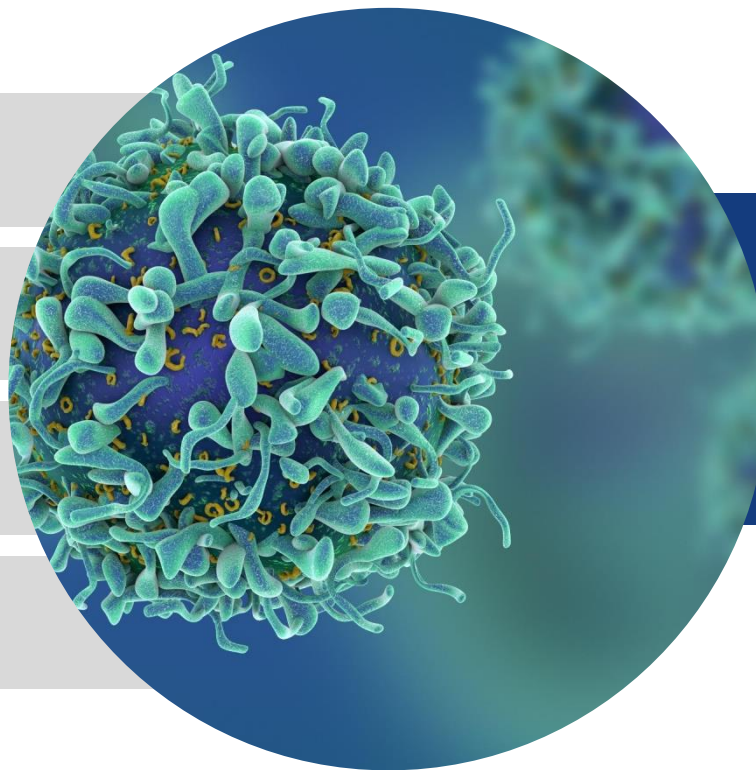
Severe complication of late-stage cancers

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**

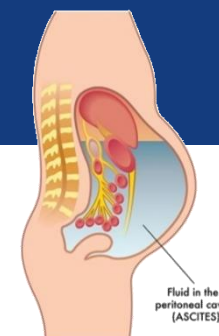
Reduces ability to undergo **anti-cancer treatment**



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

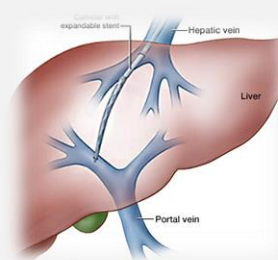
Severe limitations of existing therapies

Diet / Diuretics



Resistance,
Complications

Transjugular Intrahepatic Portosystemic Shunt (TIPS)



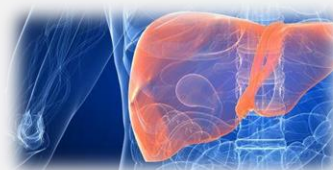
Complications,
Contraindications

Drainage (“Large Volume Paracentesis / LVP”)



Painful, Poor Quality of
Life, Short Term Benefit

Liver transplantation



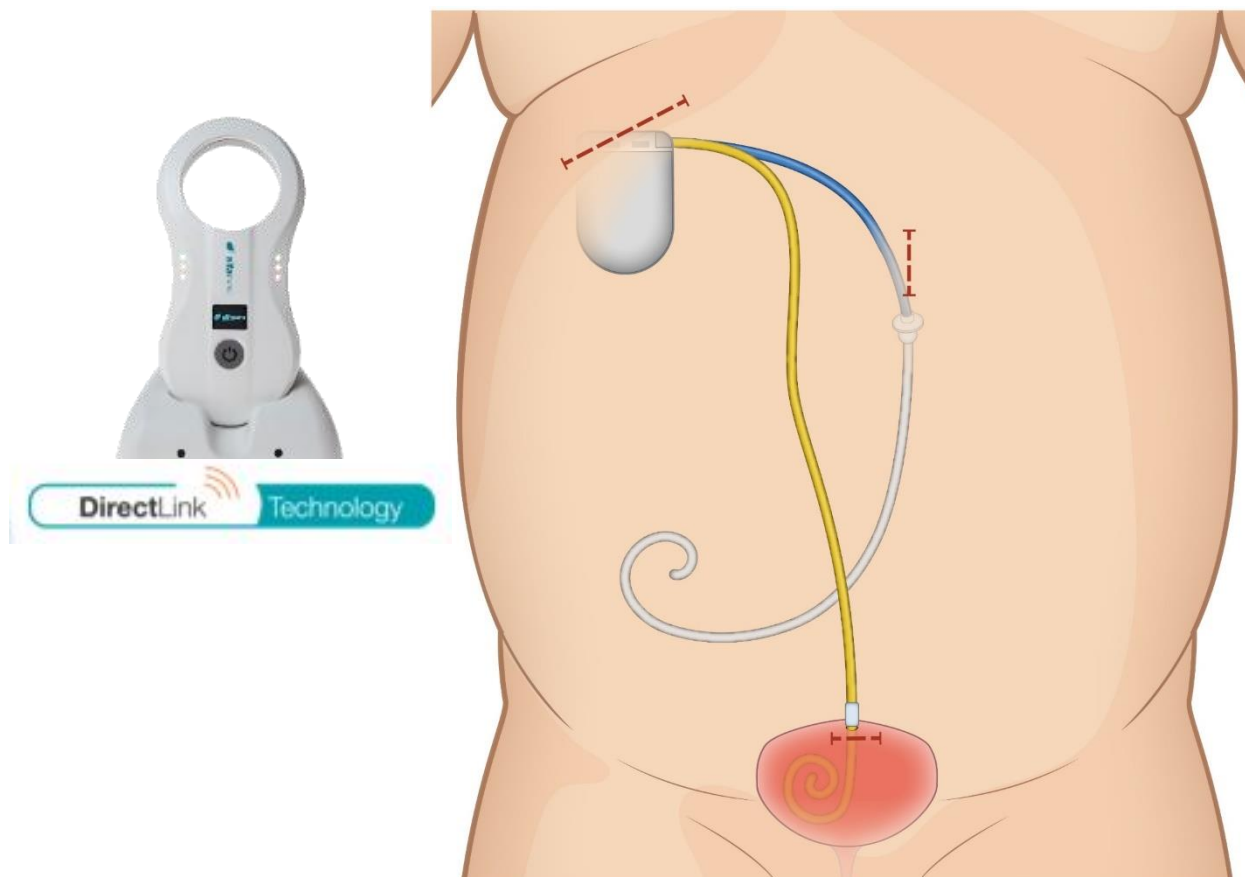
High Cost,
Limited Availability

alfapump®



alfapump® for long-term treatment

Over 800 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**

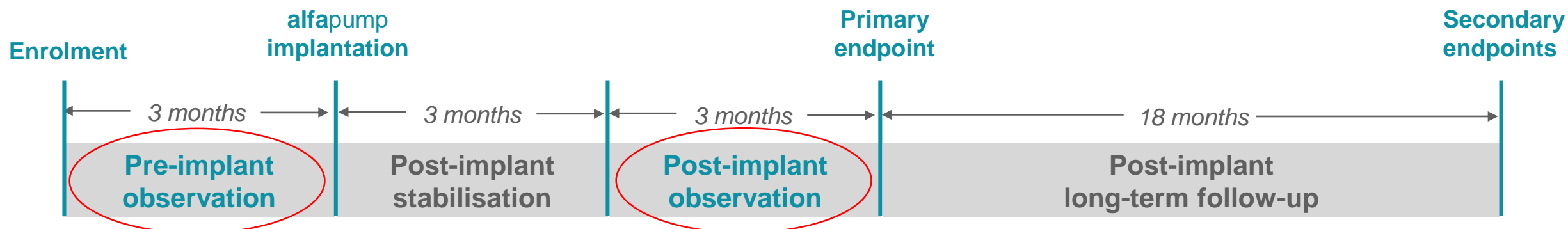
~\$1,8K / LVP⁽¹⁾
2 LVP / month
15 months

~\$25K / alfapump
~\$10K / implantation

* 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

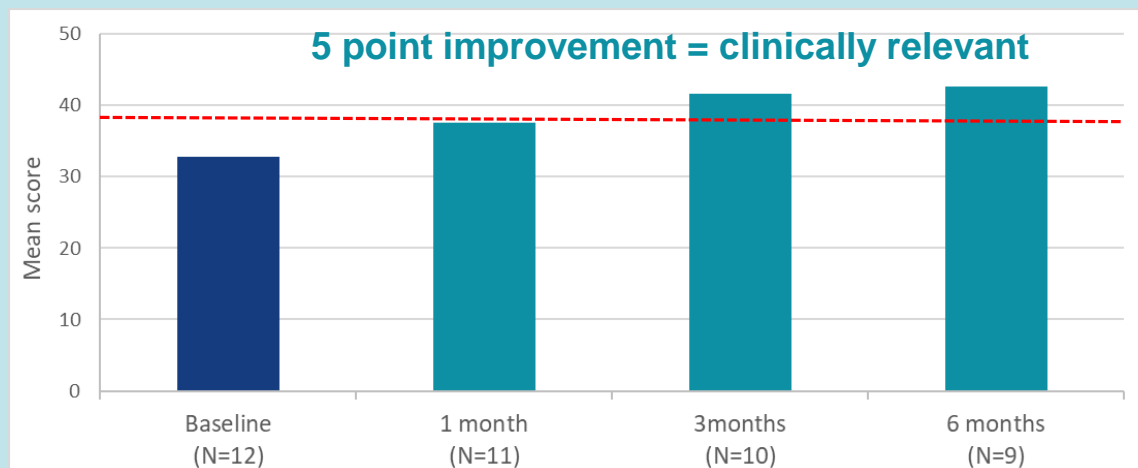
Note: Pre- and post-implant periods for this analysis of the Roll-In Cohort differ from those that will be used for the Pivotal Cohort analysis

Quality of Life: Indication of fast and persistent improvement

SF-36

*General health-
survey
questionnaire*

Physical Component Score



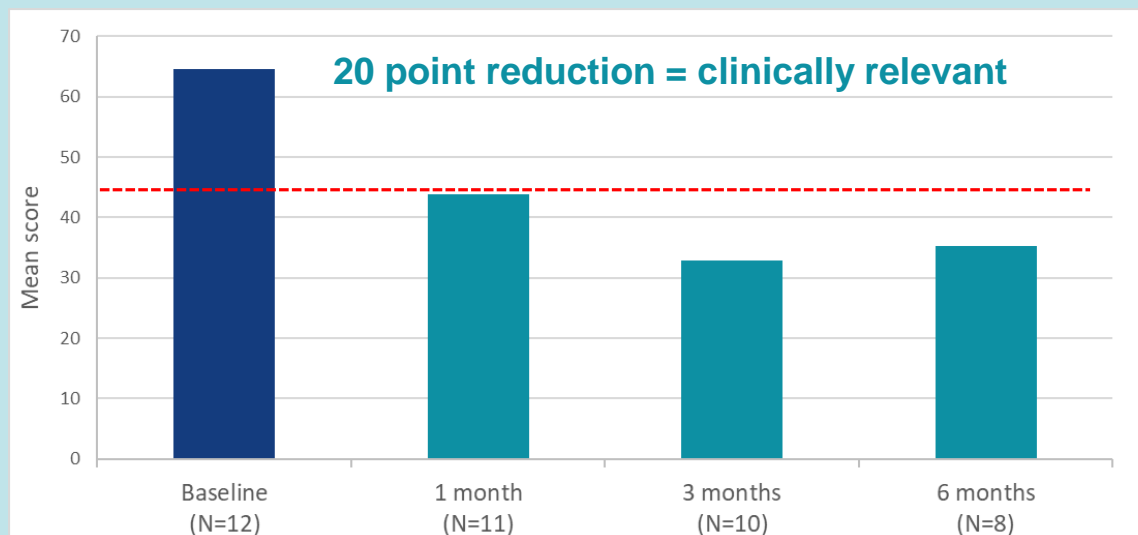
Higher is
better



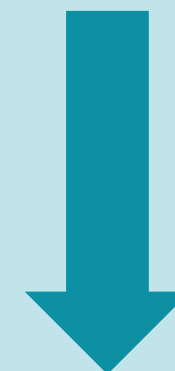
Ascites Q

*Specific health-
survey
questionnaire
for ascites*

Total Score

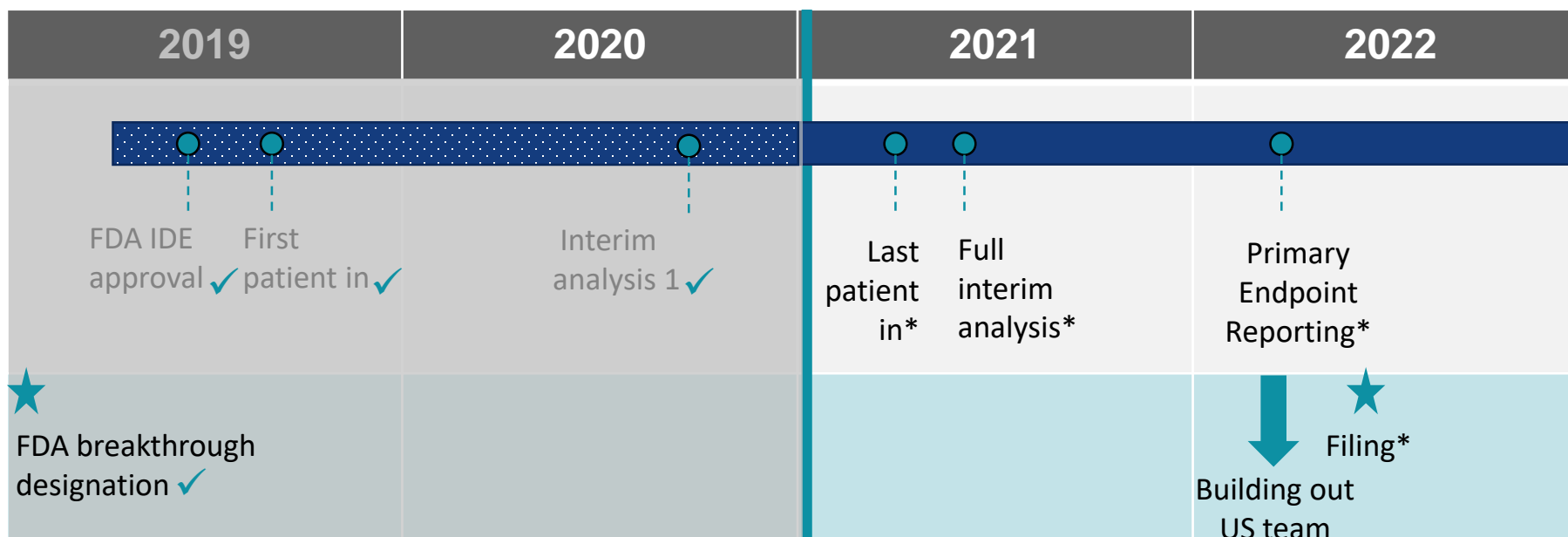


Lower is
better



Strong progress towards alfapump® US approval

Targeting announcement of primary endpoint in Q1 2022

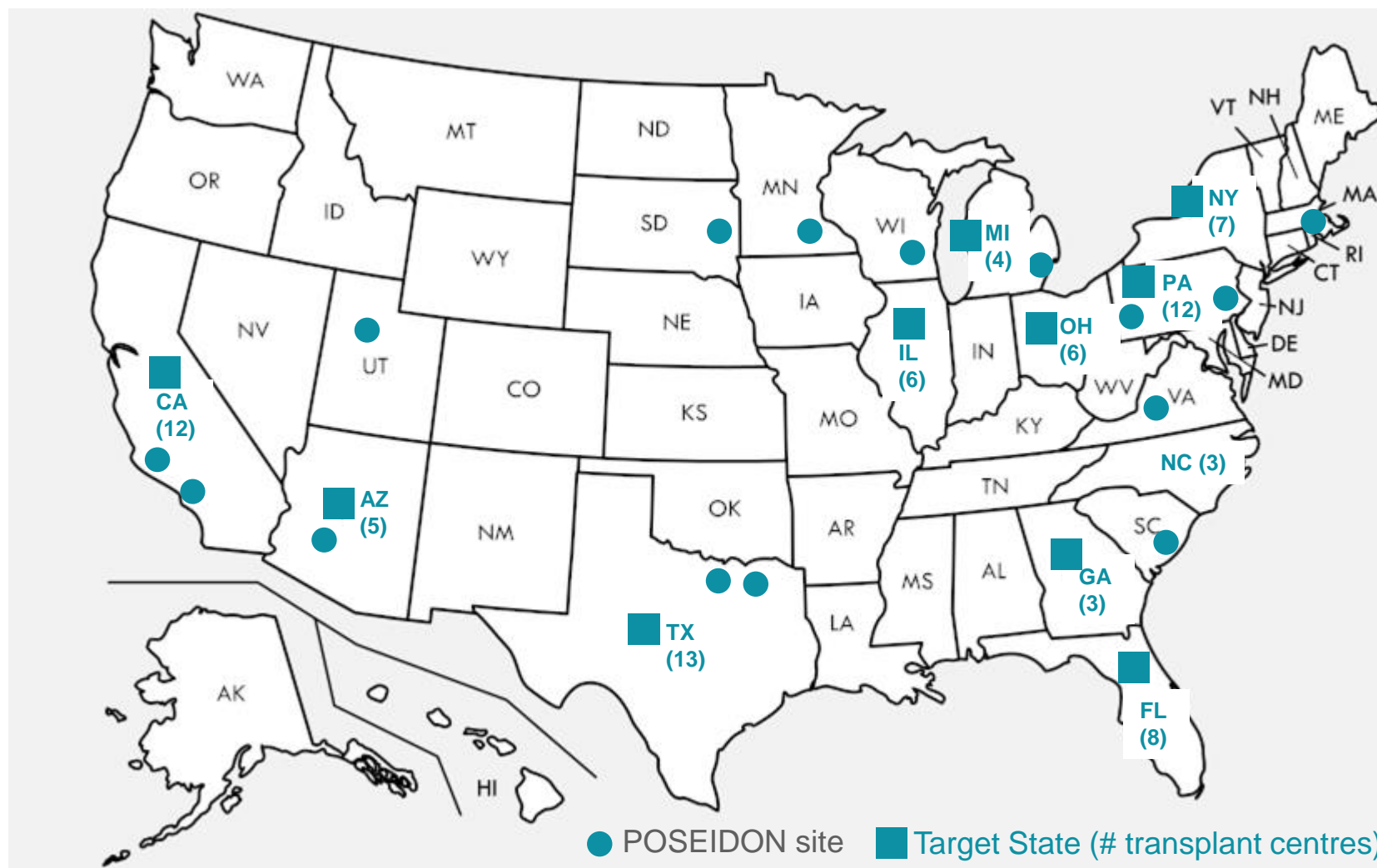


Proposed CMS rule for automatic Medicare coverage of breakthrough devices for four years post-approval

* 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

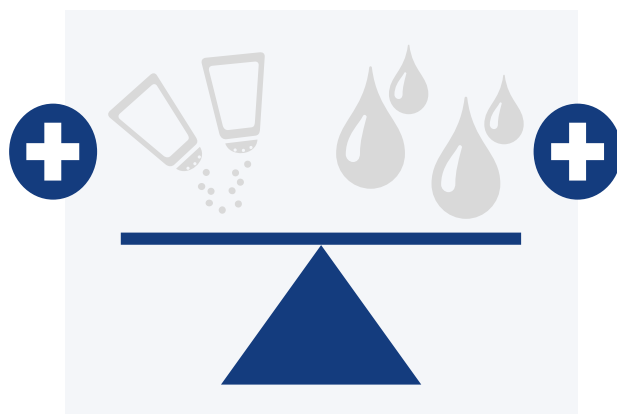


alfapump® DSR

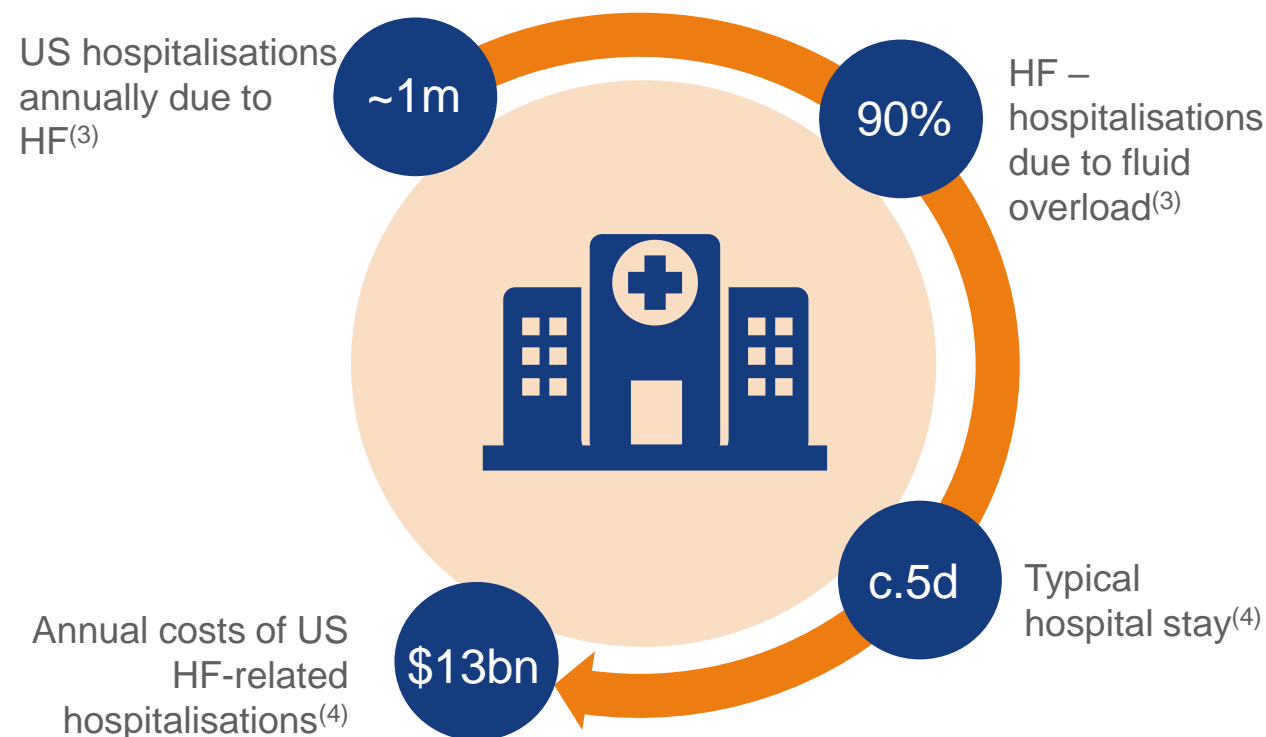
Breakthrough approach to **fluid overload in heart failure** built on proven **alfapump** platform

Diuretic-resistant fluid overload in heart failure

Key clinical challenge and driver of costs



Excess sodium drives
fluid overload



- 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”

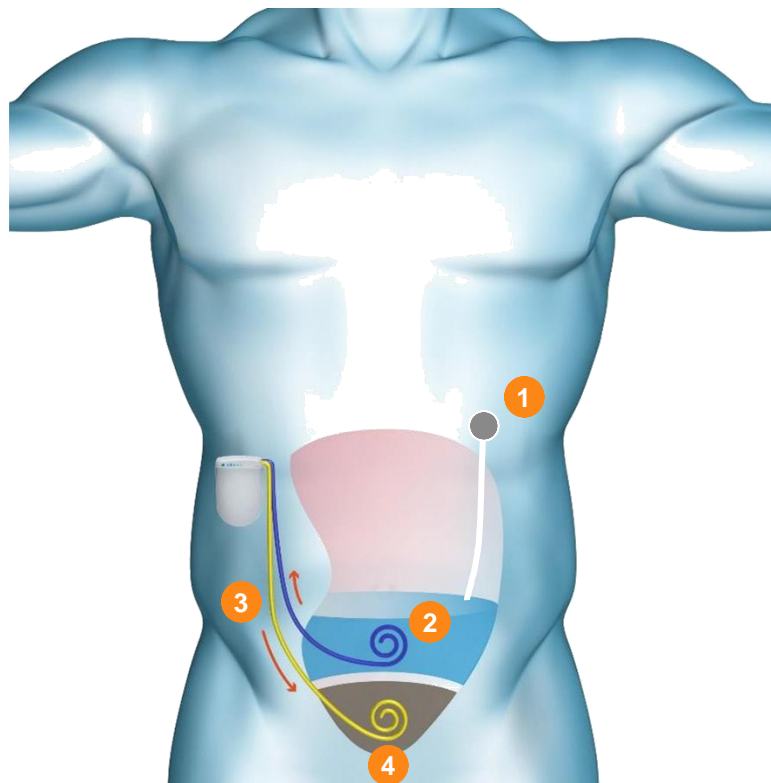
Circulation First in Human Experience with Peritoneal Direct Sodium Removal Using a Zero Sodium Solution: A New Candidate Therapy for Volume Overload

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

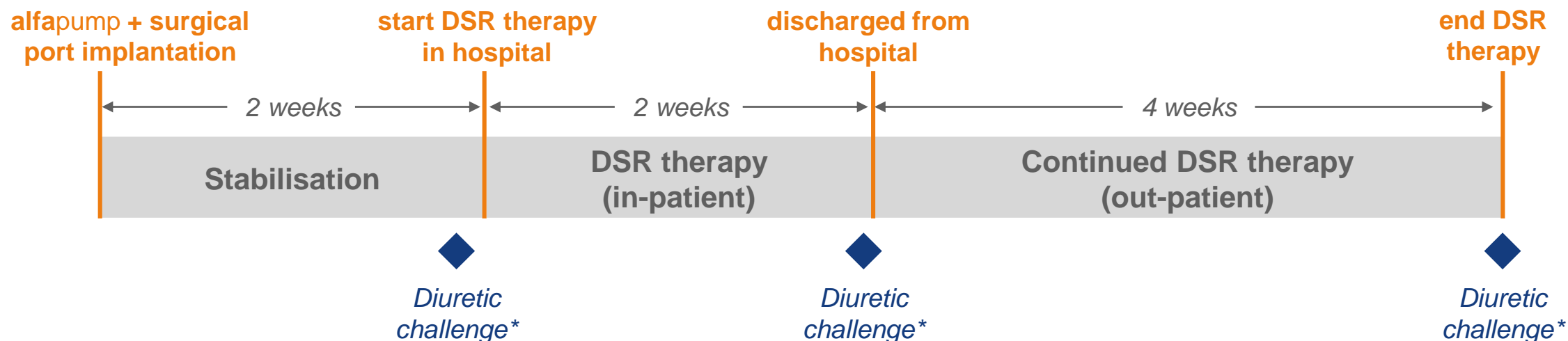


- 1 Sodium-free DSR infusate administered to peritoneal cavity via implanted port
- 2 Sodium diffuses into DSR infusate
- 3 **alfapump** pumps sodium-rich DSR infusate into the bladder
- 4 Body eliminates excess fluid through osmotic ultrafiltration and urination

*Fundamental patents to reduce fluid overload in heart failure
allowed 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 H1 2021

* intravenous dose of 40mg dose furosemide

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**
 - Assessed by 6-hour excretion of fluid and sodium following 40mg furosemide IV
 - Baseline: objectively poor diuretic response
 - End of 6-week study period: sodium excretion more than doubled (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 not just a means to remove sodium and water*
 - *Potential for intermittent dosing to restore natural kidney response - delivering a breakthrough in treatment of diuretic-resistant fluid overload in HF and other indications*

Developing high value proprietary DSR Infusate

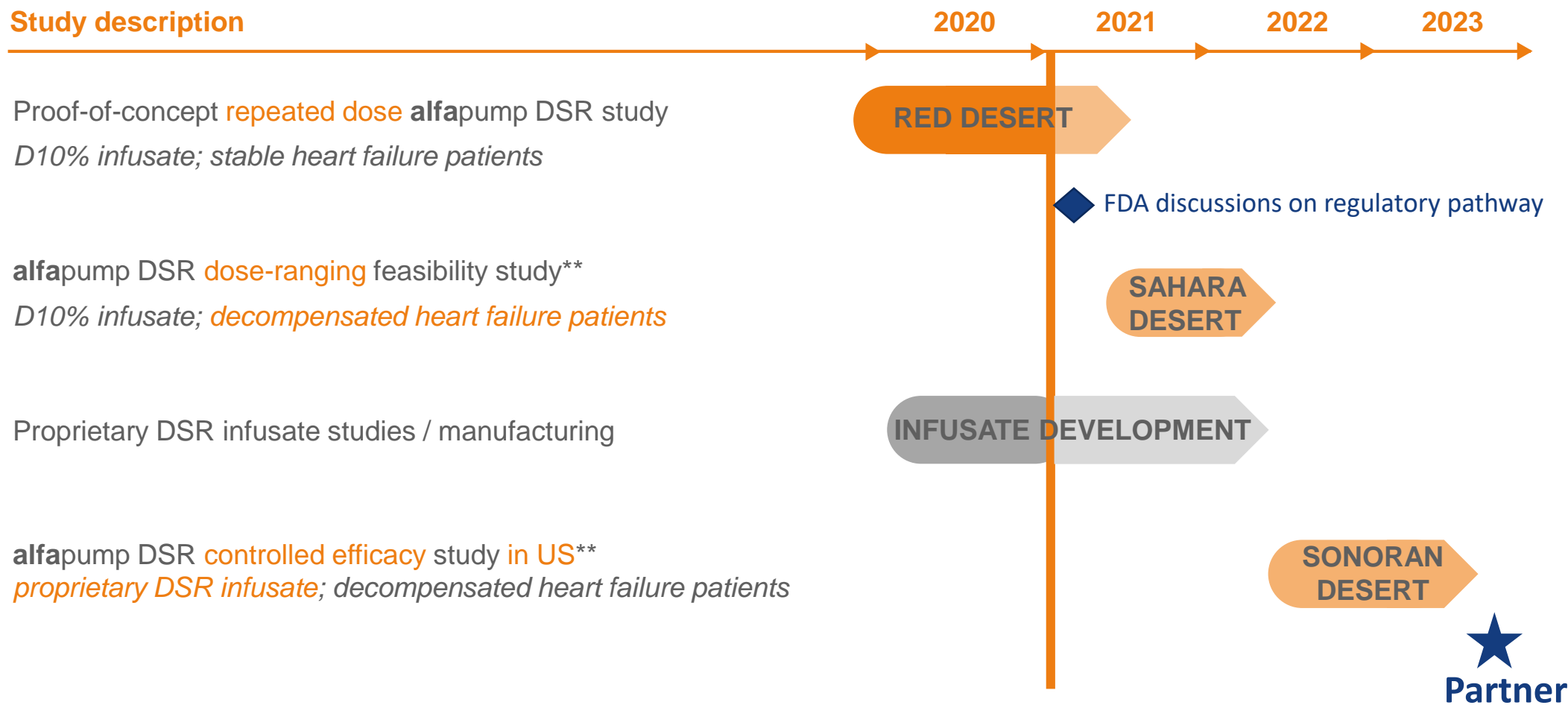
- D10% was chosen as the initial DSR infusate for fastest proof-of-concept
- We are developing our **proprietary next-generation DSR infusate**:



- ✓ Improved therapeutic profile compared to D10%
- ✓ IP protected
- ✓ Recurring revenue from high gross margin consumable

alfapump[®] DSR development strategy*

Study description



* Timelines subject to further developments related to the ongoing COVID-19 pandemic

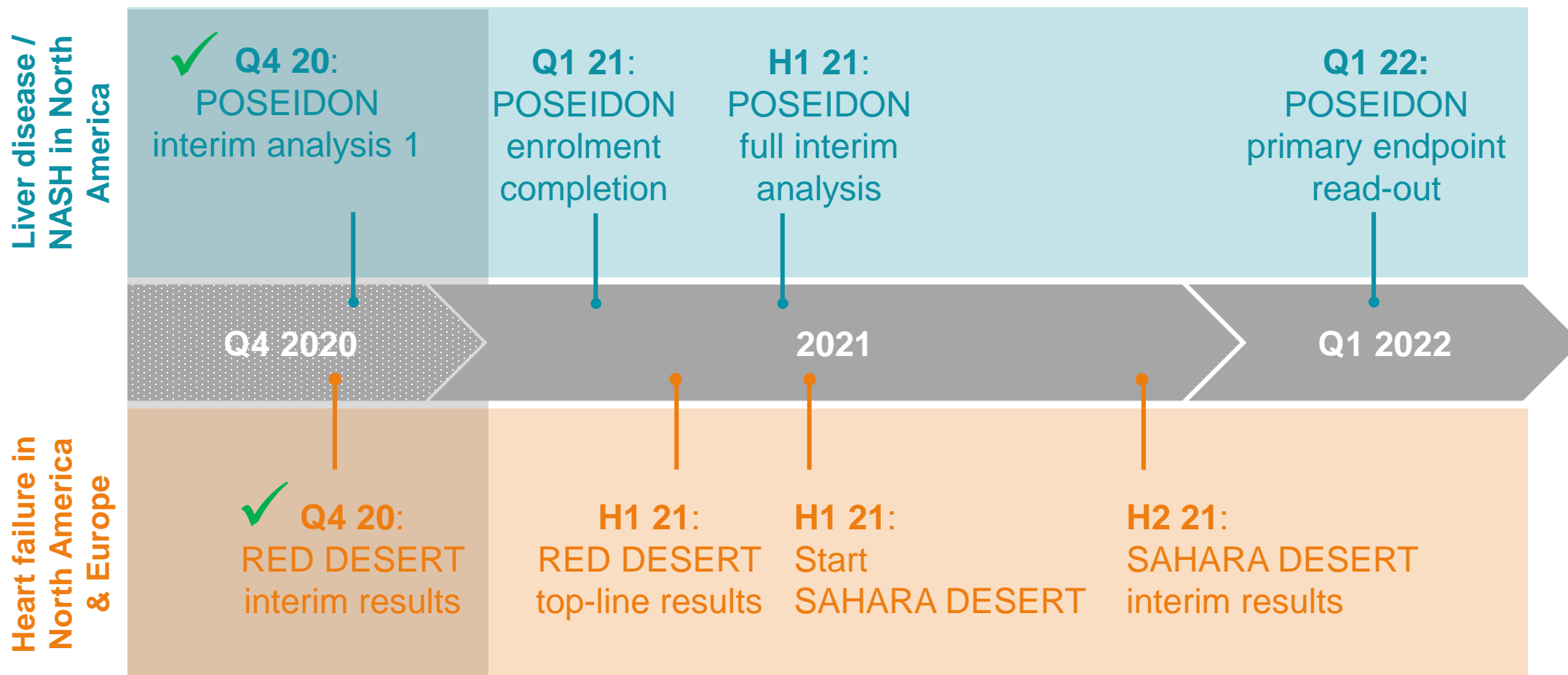
** Subject to change and/or feedback from applicable regulatory authorities



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 Gödje
Chief Medical Officer



Gijs Klarenbeek
Senior Medical Advisor



Martijn Blom
Chief Commercial Officer



Timur Resch
Global VP QM/QA/RA

Board of Directors:



Pierre Chauvineau
Board Chairman



Ian Crosbie
Chief Executive Officer



Wim Ottevaere
Director



Jason Hannon
Director



Rudy Dekeyser
Director

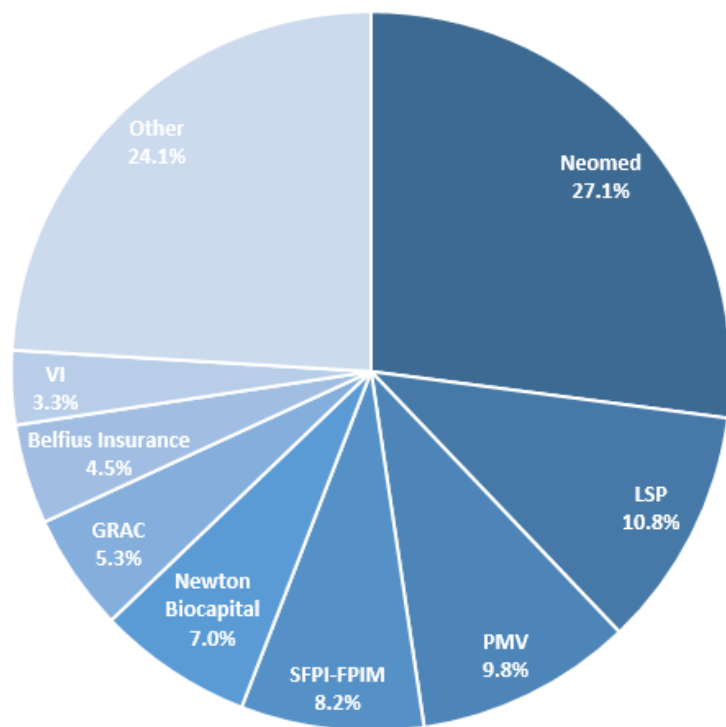


Erik Amble
Director

Shareholders base and financial overview

Ticker: SEQUA – Euronext Brussels

- Outstanding shares: 15.8M
- Outstanding share options & warrants: 1.9M authorised of which 0.9M granted



- Analysts:
 - KBC Securities – Lenny Van Steenhuyse
 - Kempen – Ingrid Gafanhão
 - Kepler Cheuvreux – Matthias Maenhaut
 - Mirabaud – Daniel Jelovcan
- Cash (30 June 2020): €14.9M
- Debt financing in July 2020: €7.3M
- Cash runway into H2 2021



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 \pm SD)	10.5 \pm 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 \pm SD)	3.4 \pm 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



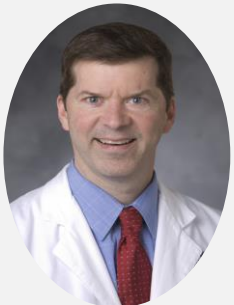
Dr. Javed Butler

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

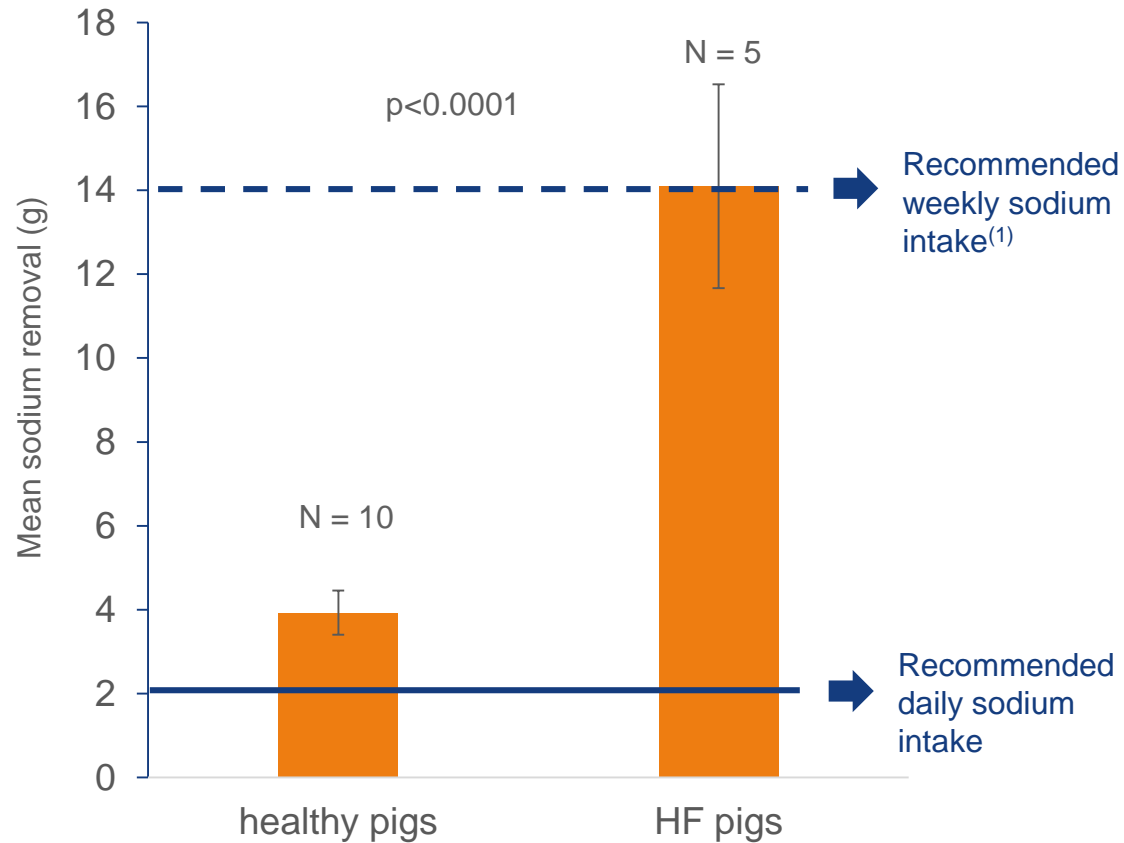
Chief of the Division of Cardiology at Tufts Medical Center
Professor of Medicine and Radiology at Tufts University School of Medicine



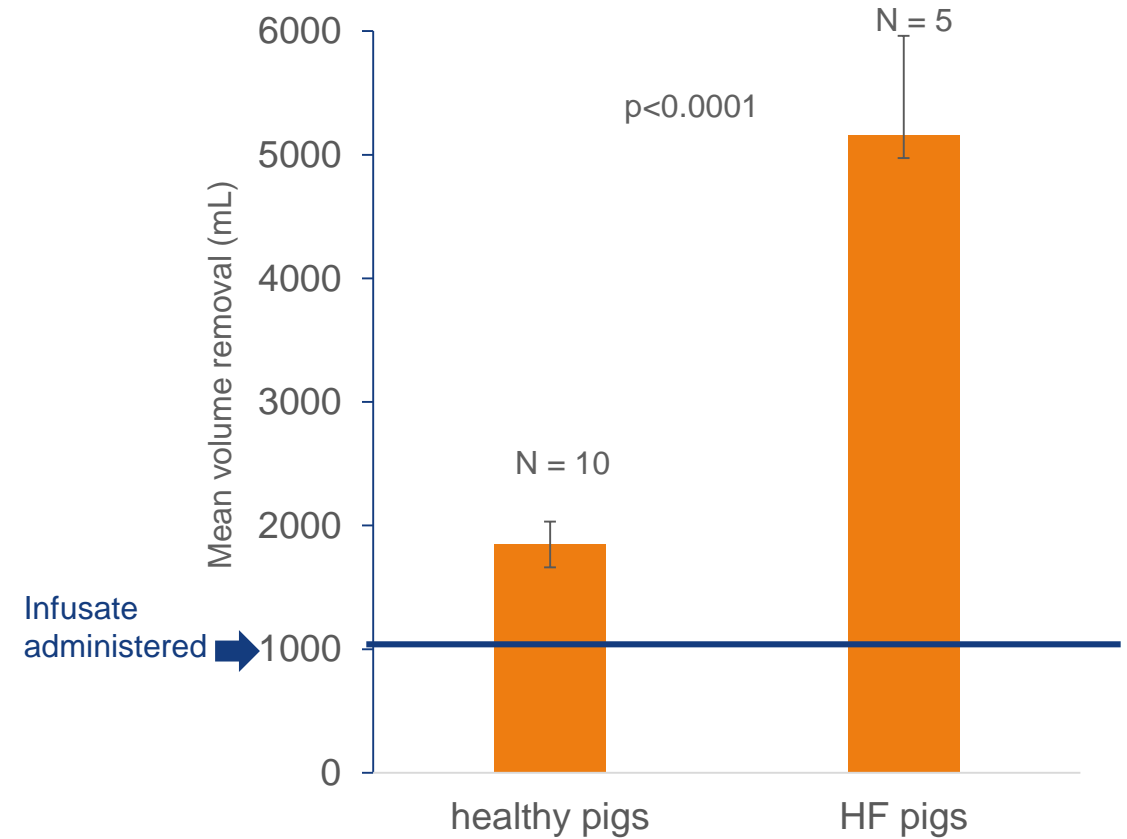
DSR pre-clinical Proof-of-Concept

Clinically relevant sodium and fluid removal

Clinically relevant removal of sodium



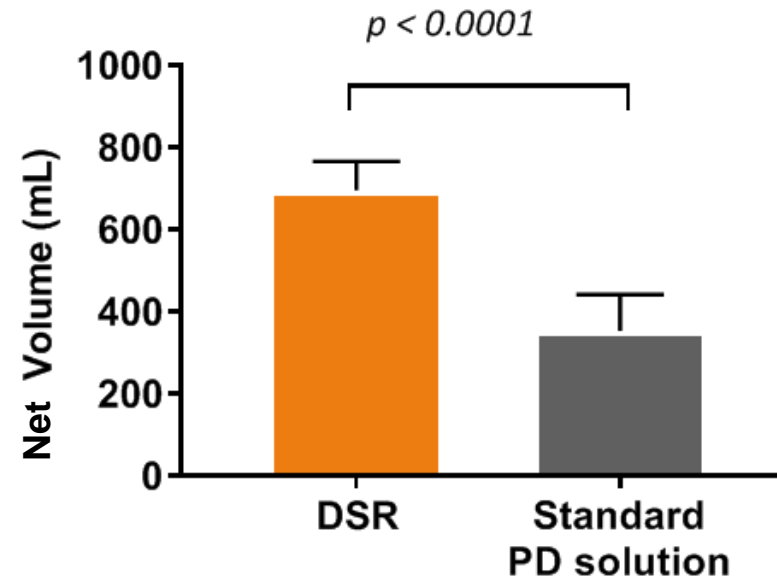
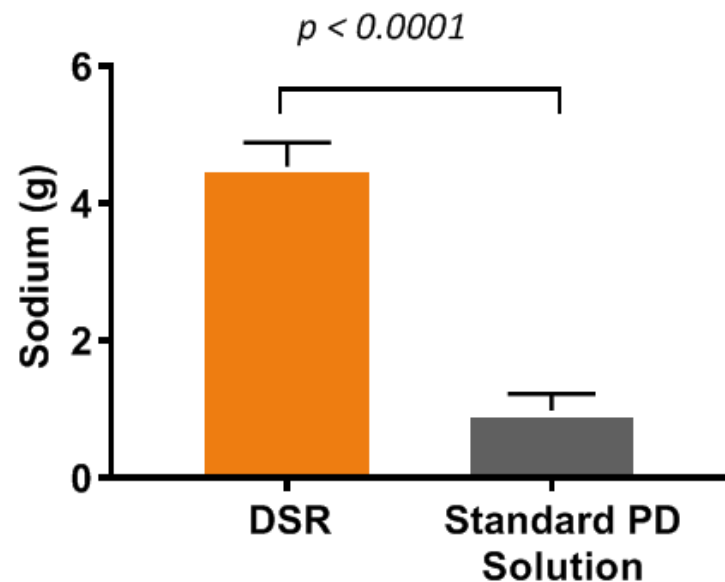
Effective fluid removal





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***



Clinical development strategy

Exciting impact on diuretic response requires additional investigation to support value of DSR therapy

RED DESERT – repeated dose study in stable heart failure patients

- Enrol up to five additional patients, with top-line data expected in H1 2021

SAHARA DESERT – dose-ranging study in decompensated heart failure patients

- Move into decompensated heart failure patients with residual congestion
- Dose ranging to learn more about improvement in diuretic response and durability of effect
- Key learnings to be taken into US controlled efficacy study
- D10% as DSR infusate

SONORAN DESERT - US study vs. stand of care with proprietary DSR infusate

- Controlled versus standard of care, in decompensated patients with residual congestion
- Treatment algorithm built upon learnings from SAHARA DESERT
- Paves the way and de-risks FDA pivotal study
- Sequana Medical proprietary DSR infusate



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