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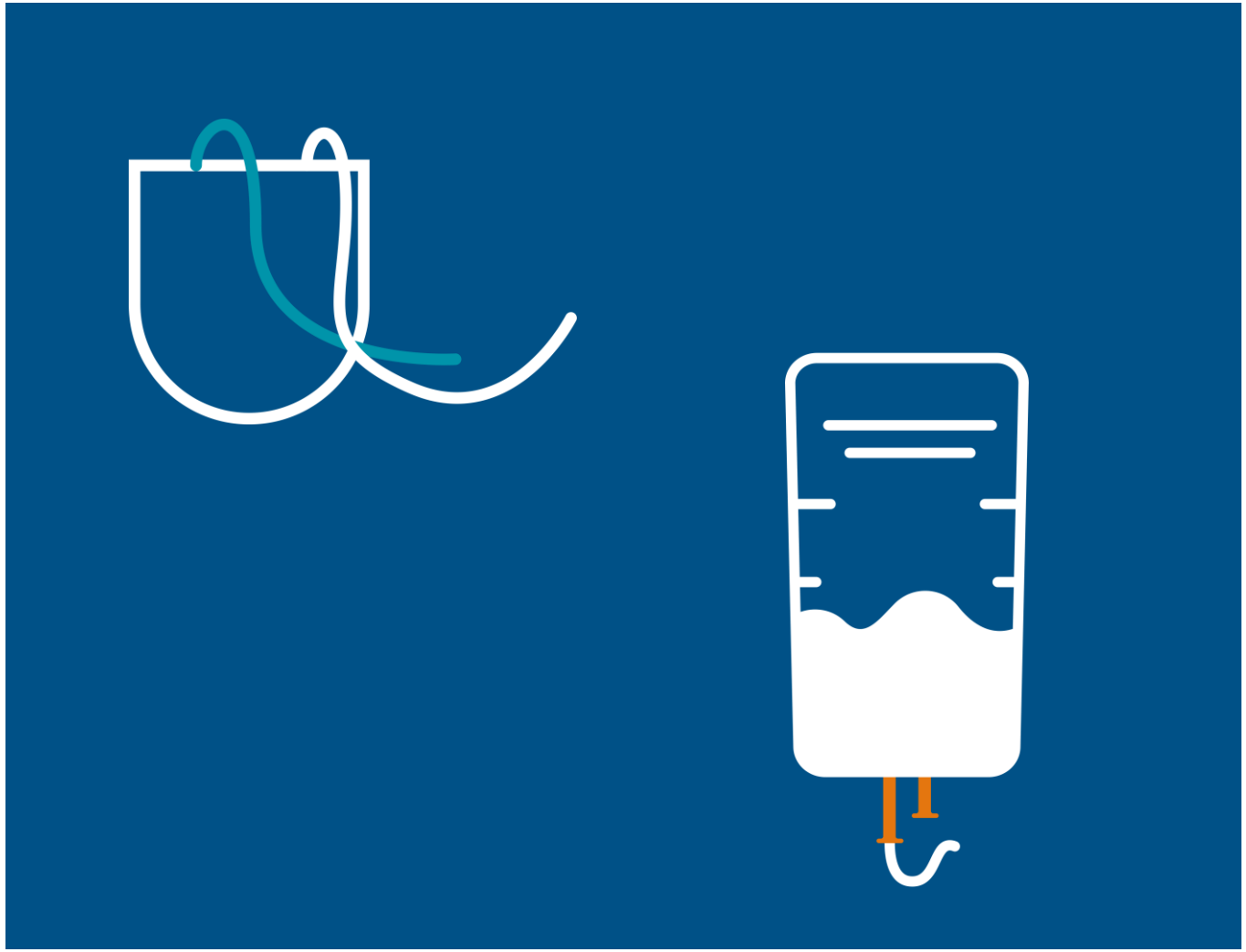

Pioneers in the treatment of fluid overload

Transforming lives in
liver disease, heart failure & cancer

Investor presentation – December 2023

Euronext: SEQUA.BR

Disclaimers

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Regulatory disclaimer:

- The **alfa**pump® system has not yet received regulatory approval in the United States and Canada. Any statement in this presentation about safety and efficacy of the **alfa**pump® system does not apply to the United States and Canada. In the United States and Canada, the **alfa**pump® system is currently under clinical investigation (POSEIDON Study) and is being studied in adult patients with refractory or recurrent ascites due to liver cirrhosis.
- 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. There is no link between DSR® therapy and ongoing investigations with the **alfa**pump® system in Europe, the United States or Canada.

General disclaimer:

- Sequana Medical is closely following the evolution of macroeconomic conditions, the geopolitical situation in Ukraine and 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:

- **alfa**pump® and DSR® are registered trademarks.

Targeting large markets with strong growth

Tackling significant unmet medical need in liver disease and heart failure

alfapump – treating recurrent & refractory ascites due to liver cirrhosis

- Successful North American pivotal study – primary endpoints met, strong clinical profile
- FDA breakthrough device status; approved in EU
- PMA filing planned for Q4 2023, FDA approval anticipated in H2 2024
- Addressable market of over $2.5 billion by 2035(1) – priority target market of $500 million at launch
- Direct sales in US & Canada; commercial team of 50
- Strong reimbursement profile, supporting price of $25K+, 75% gross margin

DSR – novel treatment for cardiorenal syndrome in heart failure

- Clinical proof-of-concept as disease-modifying drug therapy
- Low development risk, favourable safety profile & strong IP
- US Phase 1/2a randomized controlled study underway; positive data from first three patients
- Over $9 billion addressable market in US(2)
- Partnering based on US Phase 1/2a readout planned for 2025

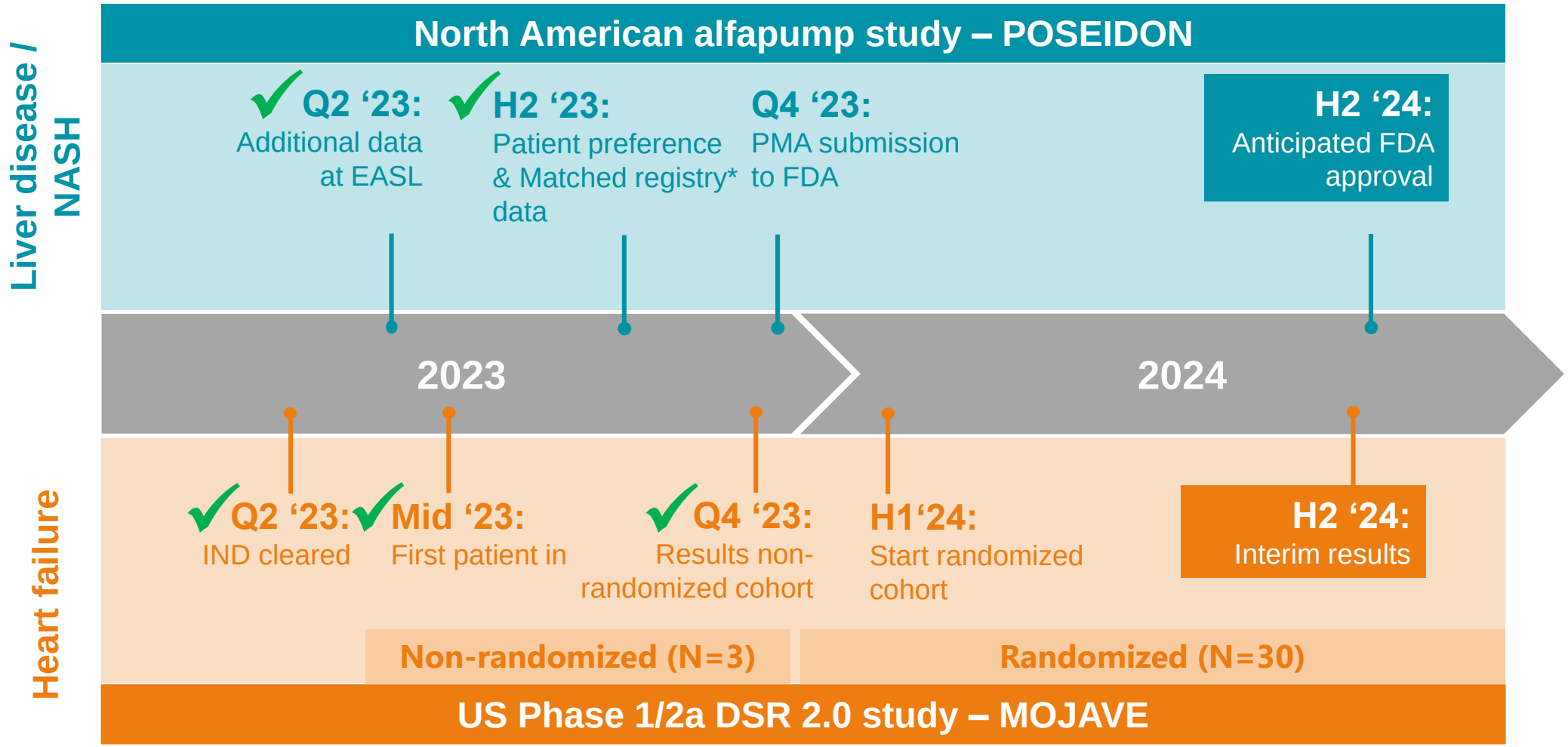
Growth in liver cirrhosis due to NASH and tackling cardiorenal syndrome in heart failure drives tremendous commercial opportunity

*Source 1: Based on US and Canada market assessment conducted by highly experienced international consulting group, estimating over 170,000 patients with recurrent or refractory ascites in North America by 2035, with estimated incidence of 60% and based on $25K for price of **alfa**pump*

Source 2: Management estimate of ~200K chronically congested HF patients hospitalized per year in the US with a US annual HF hospitalization cost per patient of $45K

***PMA:** Pre-Market Approval;*

Strong outlook for key value drivers



** Data from propensity matched interim analysis of NACSELD (North American Consortium for the Study of End-stage Liver Disease) registry vs POSEIDON pivotal cohort*

alfapump®

Proven step change in the treatment of liver refractory ascites

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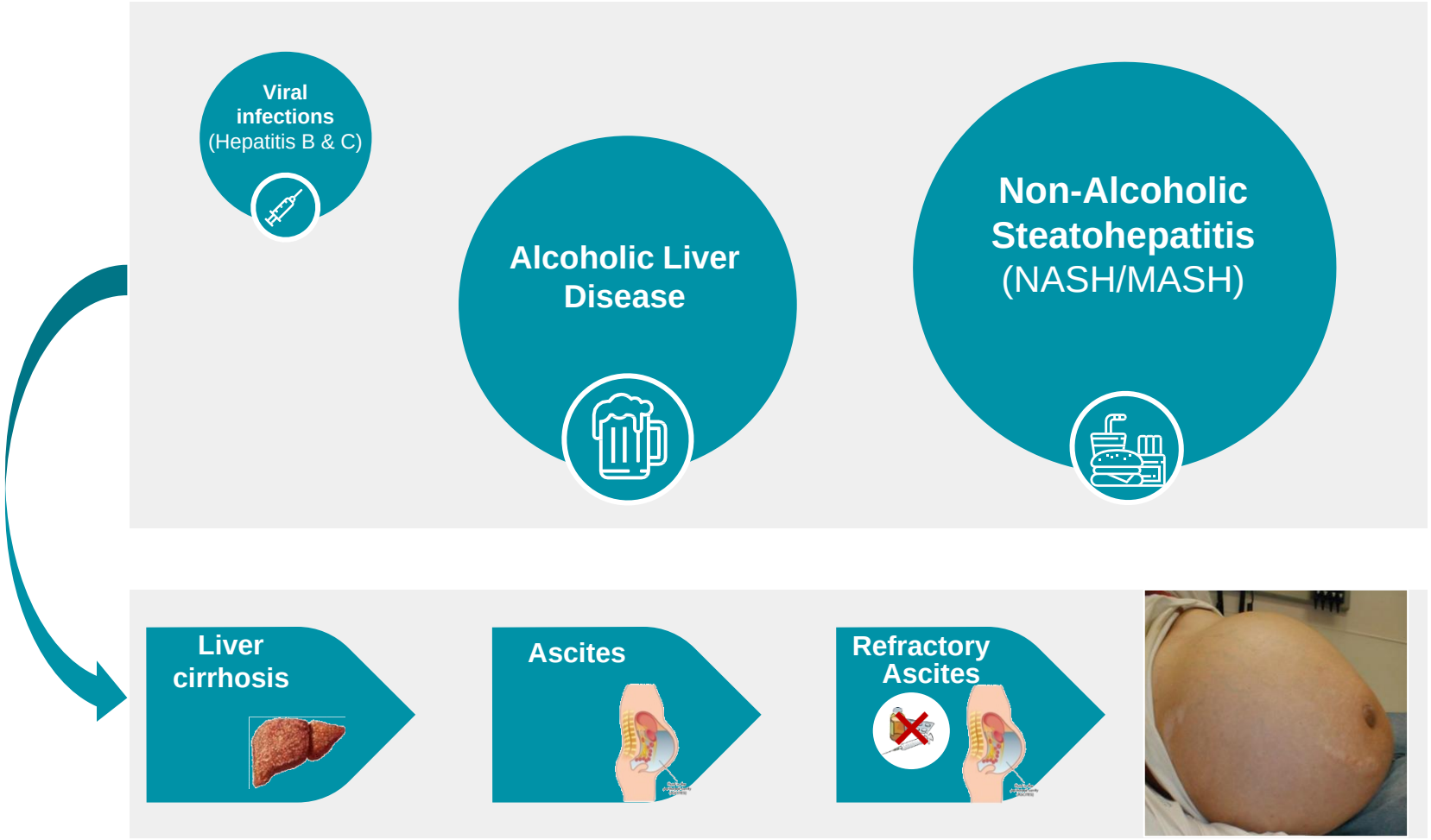
Refractory ascites – key complication of liver cirrhosis

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



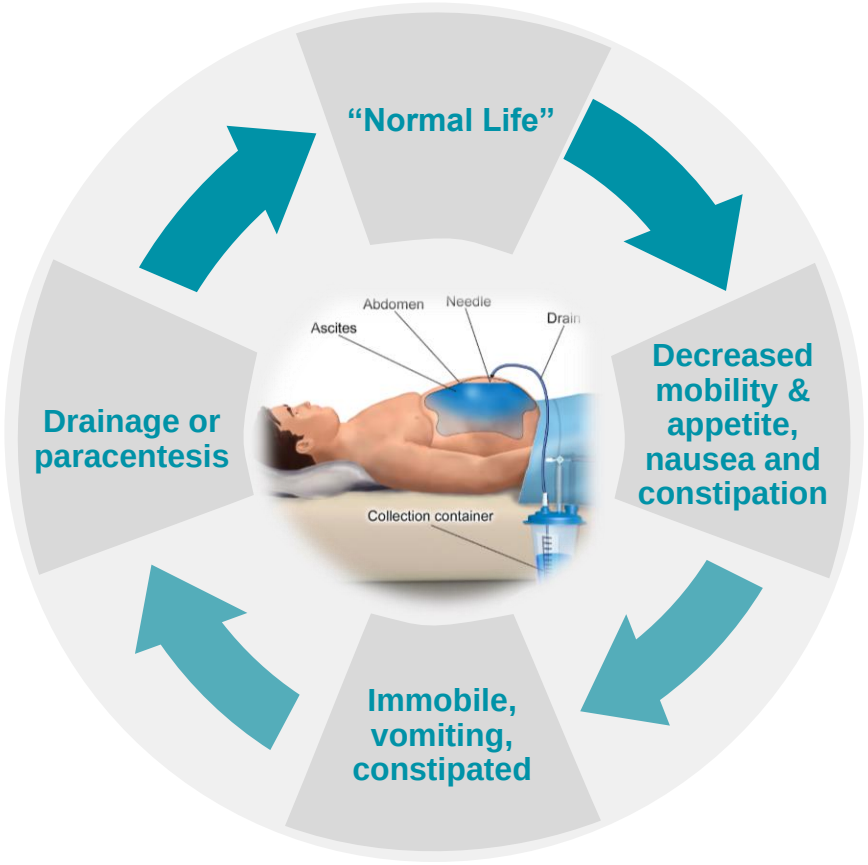
***NASH**: non-alcoholic steatohepatitis, also referred to as MASH (metabolic dysfunction-associated steatohepatitis) as per new fatty liver disease nomenclature (Hepatology, June 2023)*

Clear limitations of existing treatment options

Little innovation or new development

SoC: Paracentesis (“drainage”)

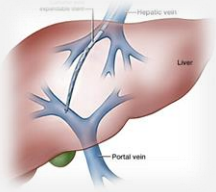
Painful, burdensome, short term benefit, QoL impact



Permanent Catheter System

External Catheter, Risk for Infections / Blockage

TIPS



Complications, Contraindications

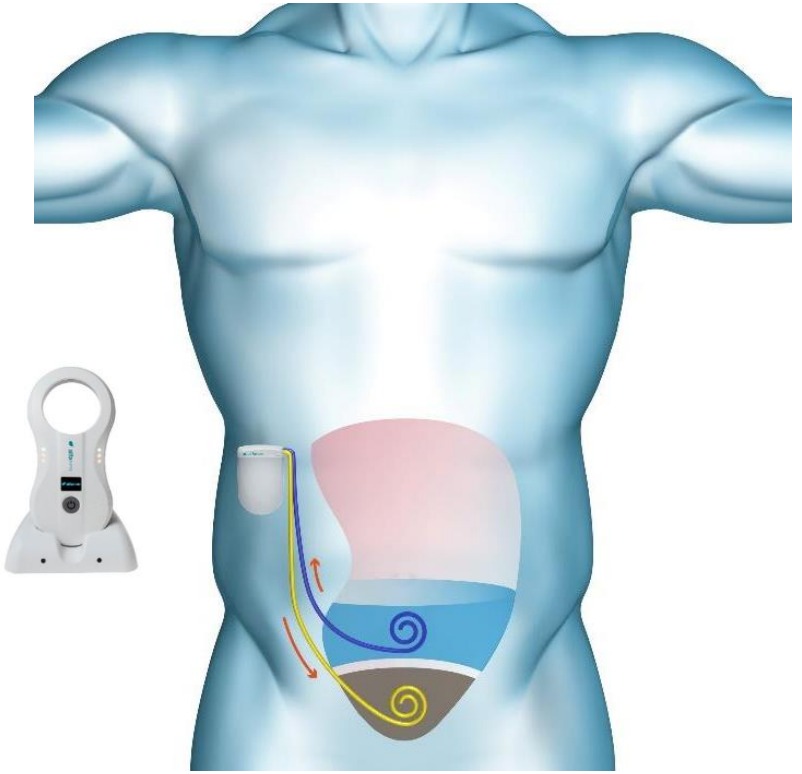
Source: Presentation of Dr. Rajiv Jalan at EASL in 2018, Large Volume Paracentesis (LVP) treatment cycle for refractory ascites

***SoC:** Standard of Care; **TIPS:** Transjugular Intrahepatic Portosystemic Shunt*

alfapump – continuous ascites removal to the bladder

Fully implanted automatic device for long term treatment

- Wireless battery charging
- Settings wirelessly adjusted
- Remote data monitoring
- Moves up to 4 litres / day



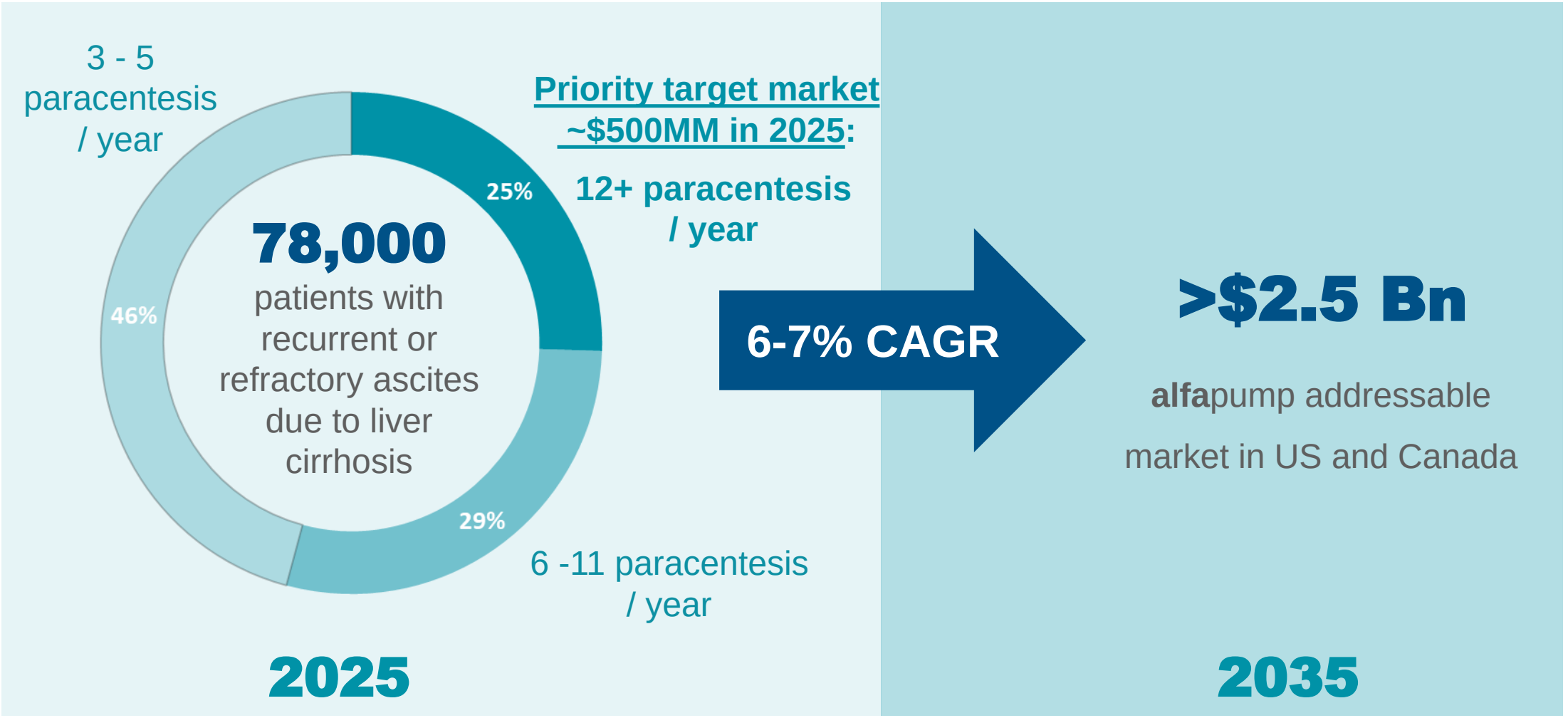
Breakthrough Device Designation

Over 1,000 systems implanted

Strong IP barriers through extensive patent portfolio & know-how

Large and strongly growing North American market

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

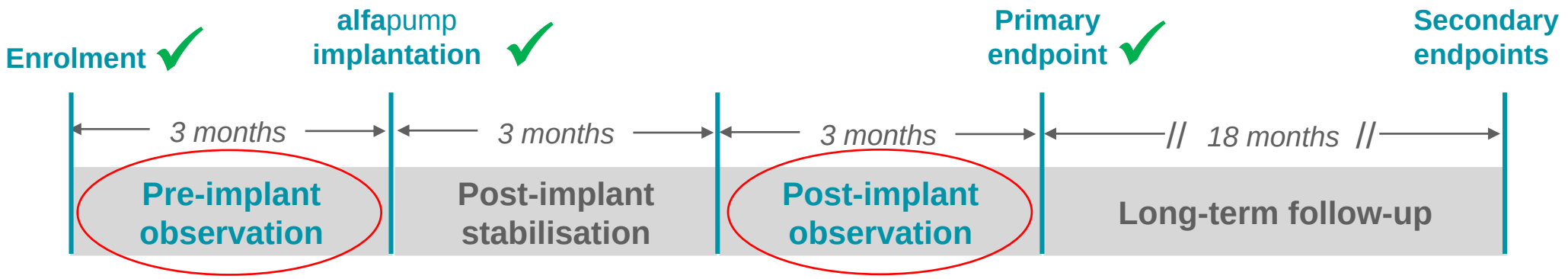


*Sources: Based on US and Canada market assessment by international consulting group, using claims analysis for commercial and CMS (Center for Medicare and Medicaid Services) patients requiring paracentesis procedure with liver disease diagnosis codes; Medicare Inpatient & Outpatient Hospital Standard Analytical Files 2019.CMS, Baltimore, MD. www.cms.hhs.gov; using incidence rate of 60% and **alfa**pump price of $25K*

***CAGR:** Compound Annual Growth Rate*

POSEIDON – Successful North American pivotal study

Pivotal Cohort of 40 patients with recurrent or refractory ascites due to liver cirrhosis



Primary effectiveness endpoints exceed predefined thresholds for study success

- **100%** median per-patient reduction in therapeutic paracentesis (N=40; p<0.001)* *vs at least 50%*
- **77% of patients** with at least 50% reduction in therapeutic paracentesis (N=40; p<0.001)* *vs at least 50%*

Primary safety endpoint data in line with expectations

- No unanticipated adverse device effects
- 6 primary safety events (3 explants due to skin erosion & 3 explants due to moderate bladder discomfort)

Clinically meaningful and statistically significant improvement in quality of life**

** Post vs Pre-implant observation period*

*** Quality of life assessed through the physical component score of SF36 and the Ascites Q score, at six months post-implant compared to baseline*

Sustained effective control of ascites and robust safety profile at 12 months post-implant

✓ Virtual elimination of needle paracentesis

- Maintaining 100% median per-patient reduction in therapeutic paracentesis (N=19, p<0.001)*

✓ Robust safety profile despite disease progression

- 2 pumps explanted (1 patient with UTI and 1 patient with wound dehiscence)**
- Number of major adverse events and serious infections in line with expectations
- Maintaining stable kidney function

✓ Maintaining clinically meaningful improvement in quality of life***

✓ Survival probability of 70% at 12 and 18 months post-implant

- Comparing favorably to literature citing only ~17% predicted survival at 12 months and ~5% at 18 months(1)

Positive pre-PMA meeting held with FDA
PMA filing on track for Q4 2023 / FDA approval anticipated in H2 2024

** 7-12 month post-implant period vs 3 month pre-implant observation period; ** during 7-12 month post-implant; *** at 12 months post-implant compared to baseline*

Source 1: Salerno et al., Gastroenterology 2007; 133:825-834; predicted survival probability for refractory ascites patients with a MELD score of 15 and receiving paracentesis

UTI: *Urinary Tract Infection*

Strong clinical messaging to patients and clinicians

Data from patient preference study and matched interim analysis of NACSELD registry with POSEIDON

- **US patients have a strong preference for the alfapump vs large volume paracentesis***
  - Reduction in paracentesis frequency and additional ascites good health days are important attributes
  - **alfa**pump benefit-risk profile from POSEIDON pivotal cohort is superior to what patients require from a novel implantable pump
- **alfapump safety profile is comparable to standard of care****
  - **alfa**pump patients benefit from significantly reduced number of paracentesis procedures and an improved quality of life without an increased risk of death or hospitalization compared to standard of care

** Patient preference study using discrete-choice experiment methodology to elicit patient preference for attributes of an implantable pump as a novel interventional treatment for ascites, N=125 US patients with comparable patient profile to pivotal cohort in POSEIDON study*

*** Comparing outcomes in terms of death, hospitalization rate and liver transplant of POSEIDON pivotal cohort (6 months post-implant) to matched patient group from NACSELD registry*

Attractive pricing with derisked reimbursement

Existing DRG payment and breakthrough device designation de-risk reimbursement

Coding – Strong existing position with potential for further upside

- Existing US hospital DRG payment for **alfa**pump procedure of $60-70K in target hospitals*
- Supports **alfa**pump price of **at least $25K** (gross margin of over 75%)
- Potential for higher payments via NTAP
- Physician CPT III coding process underway

Coverage – Breakthrough designation brings clear benefits

- Proposed TCET provides automatic coverage for 4 years with pathway to permanent coverage

Medicare will be dominant payer

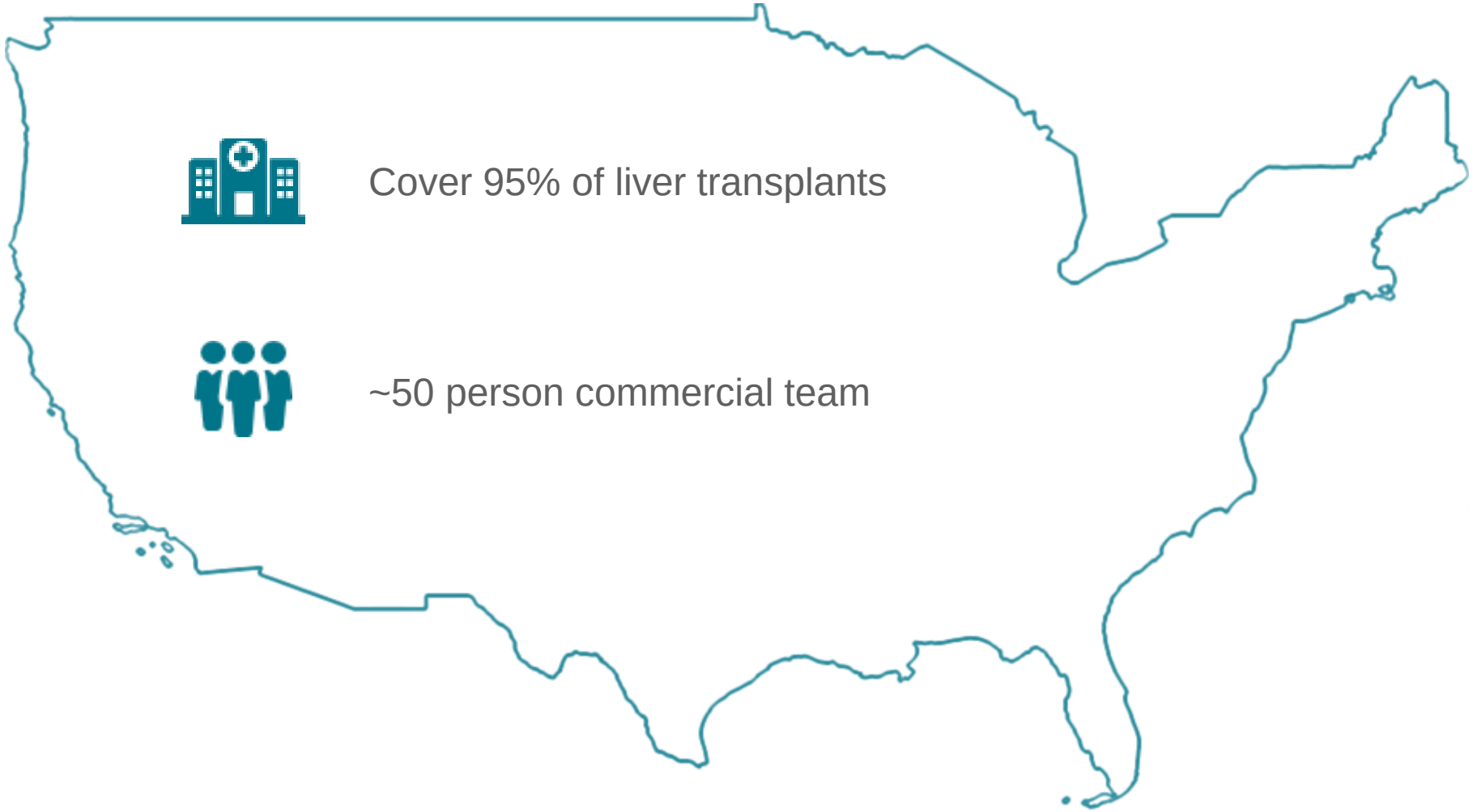
Additional potential from Veterans Affairs

On the basis of existing ICD-10 codes issued for the **alfapump, the likely DRG coding will be 423 "OTHER HEPATOBILIARY OR PANCREAS O.R. PROCEDURES", payments adjusted with Medicare inflation rates to 2025*

***DRG:** Diagnosis Related Group; **NTAP:** New Technology Add-On Payment; **CPT:** Current Procedural Terminology; **TCET:** Transitional Coverage of Emerging Technologies*

US – Go direct to 90 liver transplant centers

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



Cover 95% of liver transplants

~50 person commercial team

Source: Organ Procurement & Transplantation Network, US Dept of HHS (optn.transplant.hrsa.gov)

DSR®

Disease-modifying heart failure drug therapy tackling cardiorenal syndrome (CRS)

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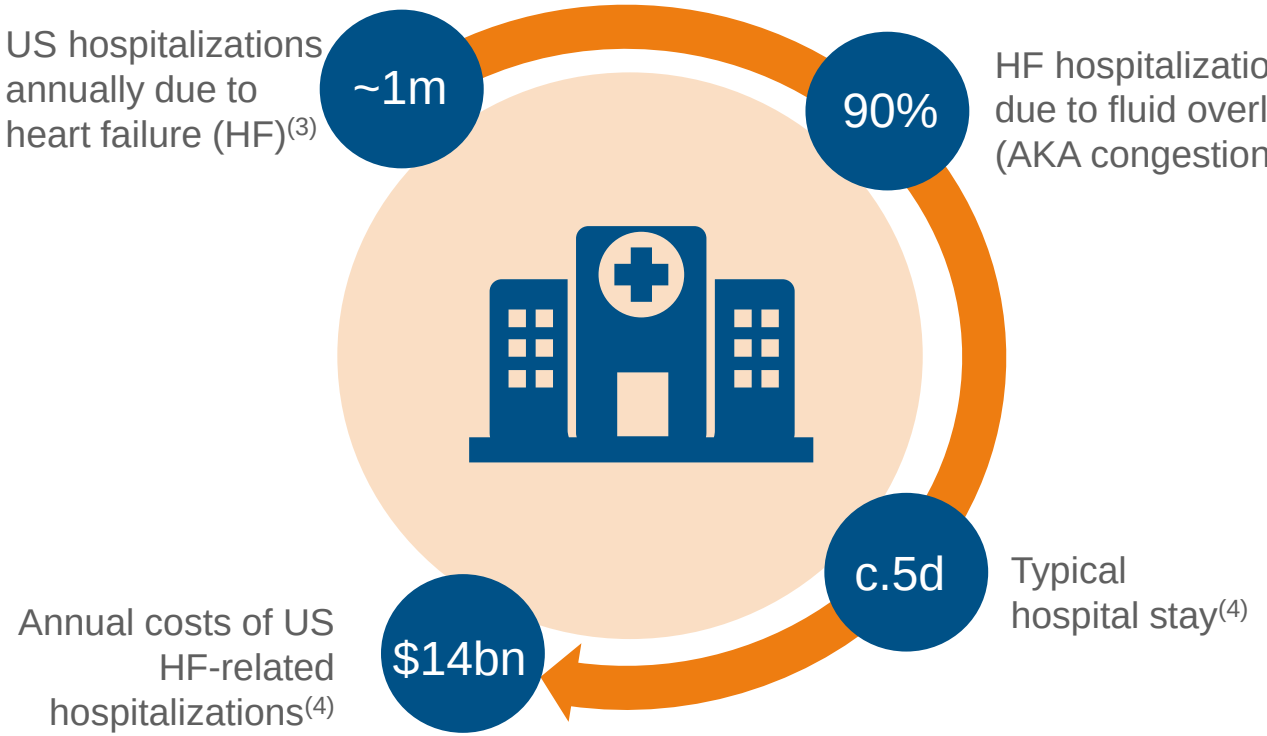
Cardiorenal Syndrome – key clinical challenge in HF

Clear need for new options to tackle congestion for sufficient time without the problems of loop diuretics

- Combined, and self-reinforcing dysfunction of heart and kidneys with hypothesised complex and interconnected mechanisms
- Clinical profile thought to manifest as self-reinforcing negative feedback cycle that is challenging to break
  - Decreased glomerular filtration, increased renal sodium avidity and congestion, despite escalating diuretic doses
- Loop diuretics are mainstay of decongestion therapy BUT exacerbate many of the core mechanisms thought to underly CRS, worsening diuretic resistance and CRS

Congestion is key driver of morbidity & hospitalization

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



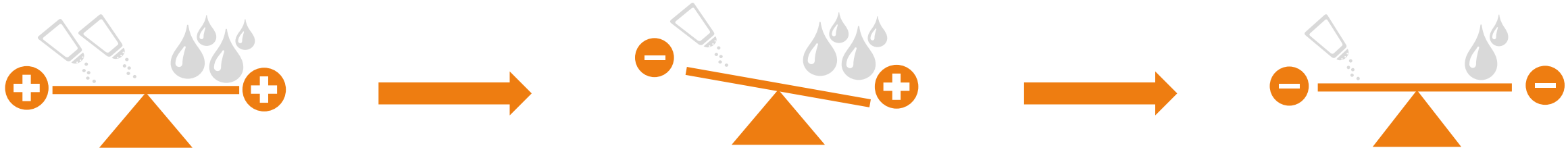
40% of heart failure patients on IV loop diuretics have a poor response(1)

24% re-admission rate at 30 days(2)

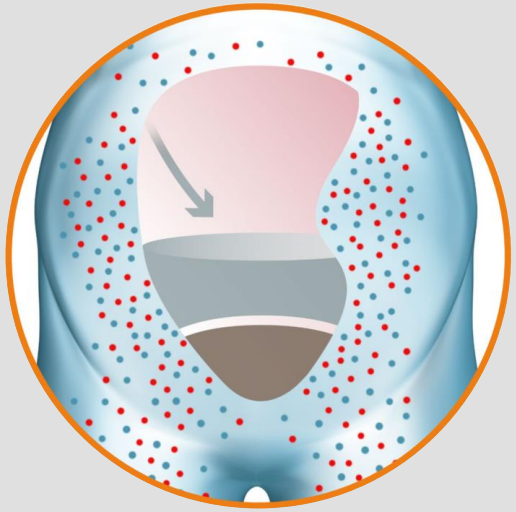
Source 1: Testani, Circ Heart Failure, 2014 & 2016; Source 2: Ross et al. (2010); Source 3: Costanzo et al., J. Am. Coll., 2007; Source 4: Urbich et al. (2020)

DSR (Direct Sodium Removal) targets key driver

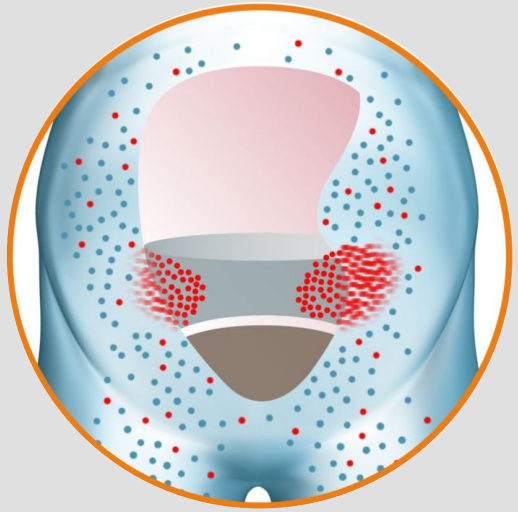
Eliminating fluid spread across the body – working in partnership with the kidneys



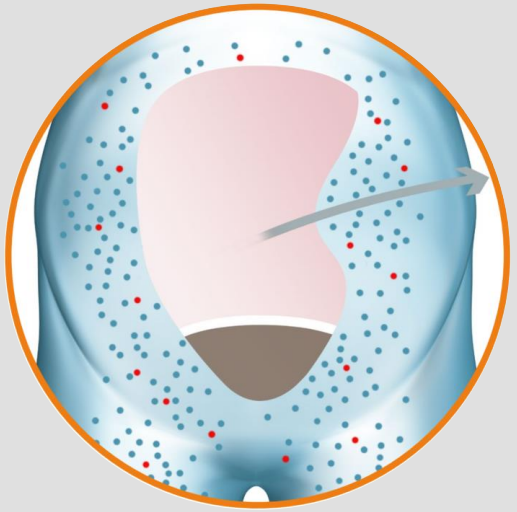
1 Sodium-free DSR product administered to peritoneal cavity



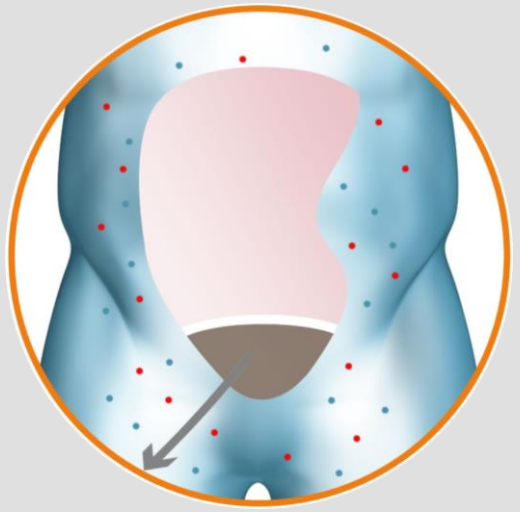
2 Sodium diffuses from body into DSR product



3 DSR product + extracted sodium removed from body



4 Body eliminates free water to restore sodium balance, reducing the fluid overload



- water
- sodium

Fundamental patents to reduce fluid overload in heart failure patients granted in US, Europe & China

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Breaking the CRS vicious cycle improves outcomes

Rapid and effective decongestion PLUS improvement in cardio-renal status

Clinical proof-of-concept from RED DESERT and SAHARA studies

- ✓ Complete replacement of loop diuretics with safe, rapid and effective decongestion and maintenance of euvolemia
- ✓ Normalization of renal diuretic-response & long lasting reduction in loop diuretic needs post-DSR
- ✓ Improvement in renal function
- ✓ No significant increase in renin or aldosterone (after adjustment for weight loss during decongestion)

Leading to improved clinical outcomes

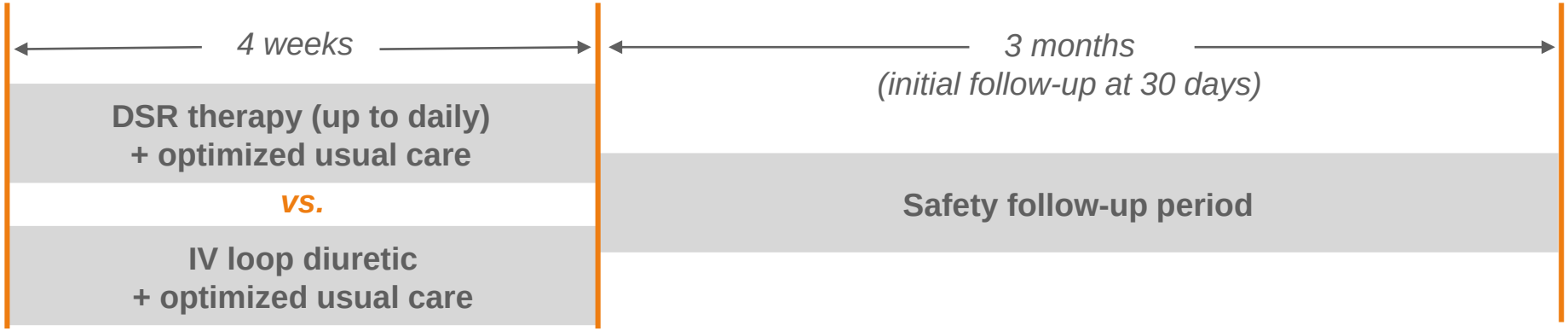
- ✓ No congestion-related heart failure re-hospitalizations
- ✓ One class improvement of NYHA status
- ✓ Over 75% reduction in predicted one-year mortality*

** Based on Seattle Heart Failure Model*

***NYHA**: New York Heart Association classification (data collected outside study protocols of RED DESERT and SAHARA)*

MOJAVE – Phase 1/2a randomized controlled US study

Seeking to replicate RED DESERT and SAHARA positive results in US patients using DSR 2.0



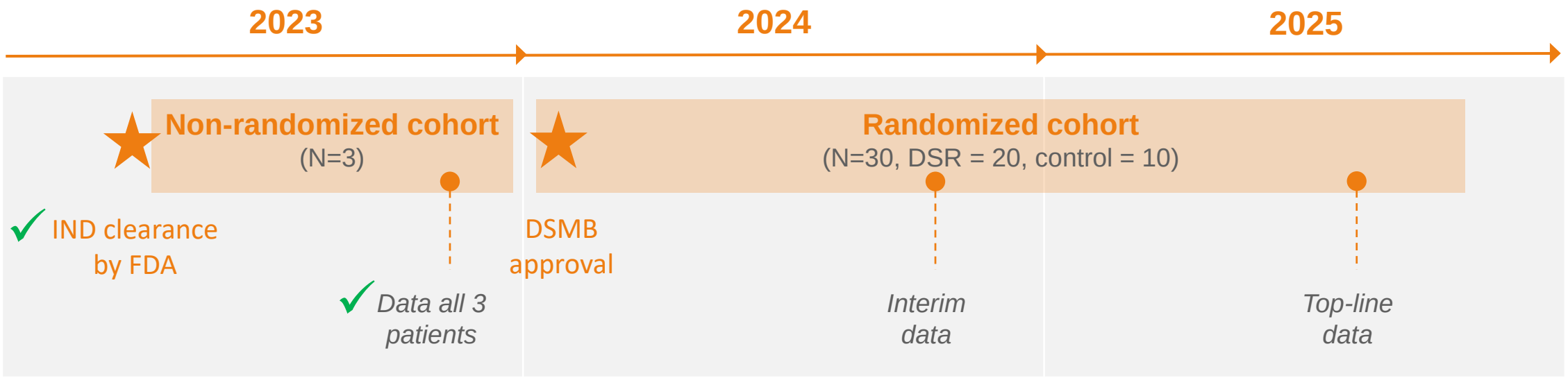
Endpoints

- **Safety:** rate of adverse and serious adverse events
- **Efficacy:** improvement in diuretic response (6-hour urine sodium output)
- **Exploratory:** change in weight (volume status), creatinine (renal function), natriuretic peptides (heart function), NYHA functional class, number of HF-related re-hospitalizations

Very strong data from three non-randomised patients

Data from first randomised cohort planned for H2 ’24; top-line data expected H2 ’25 for partnering

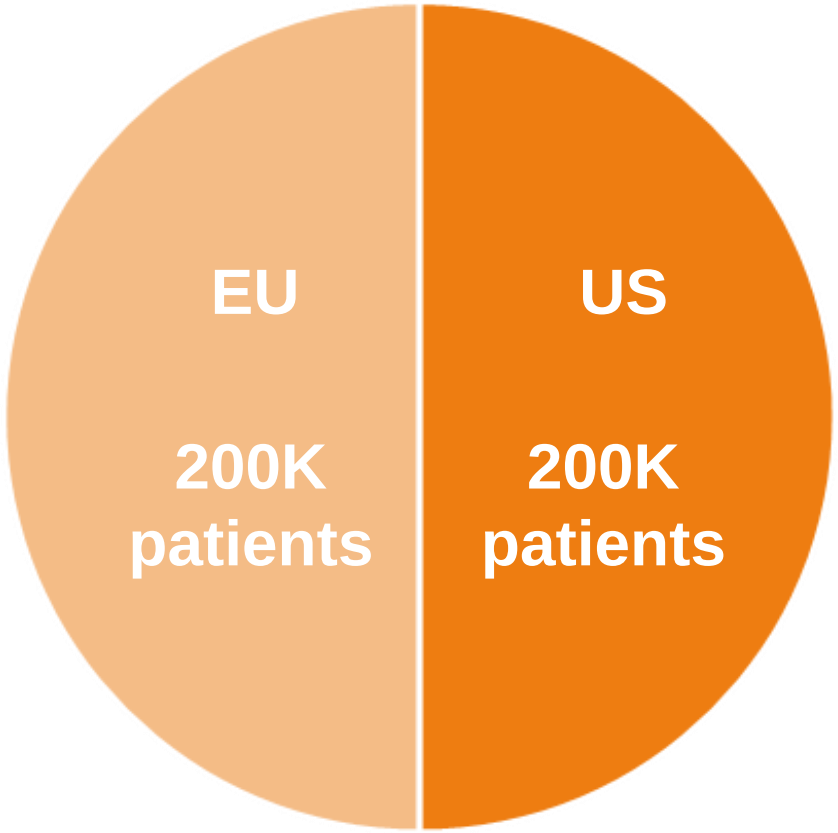
- Safe and effective maintenance of euvolemia without the need for loop diuretics
- Considerable benefit in cardiorenal health
- Dramatic improvement in diuretic response* and loop diuretic requirements** post-DSR therapy



** Mean increase of 324% in six-hour urinary sodium excretion after 4-week DSR therapy vs baseline*
*** Respectively 97%, 100% and 100% reduction in furosemide equivalent dose at 11.4, 6.4 and 1.4 weeks after 4-week DSR therapy vs baseline*

Multi-billion commercial opportunity

~400K chronically congested HF patients hospitalized per year in the US and EU (“frequent flyers”)



$45K

US annual HF hospitalization cost per patient

>$9 Bn

DSR addressable market in **US**

Potential for premium DSR pricing through reduced hospitalization and improved survival

Outlook

Strong near term value drivers with clear long term potential

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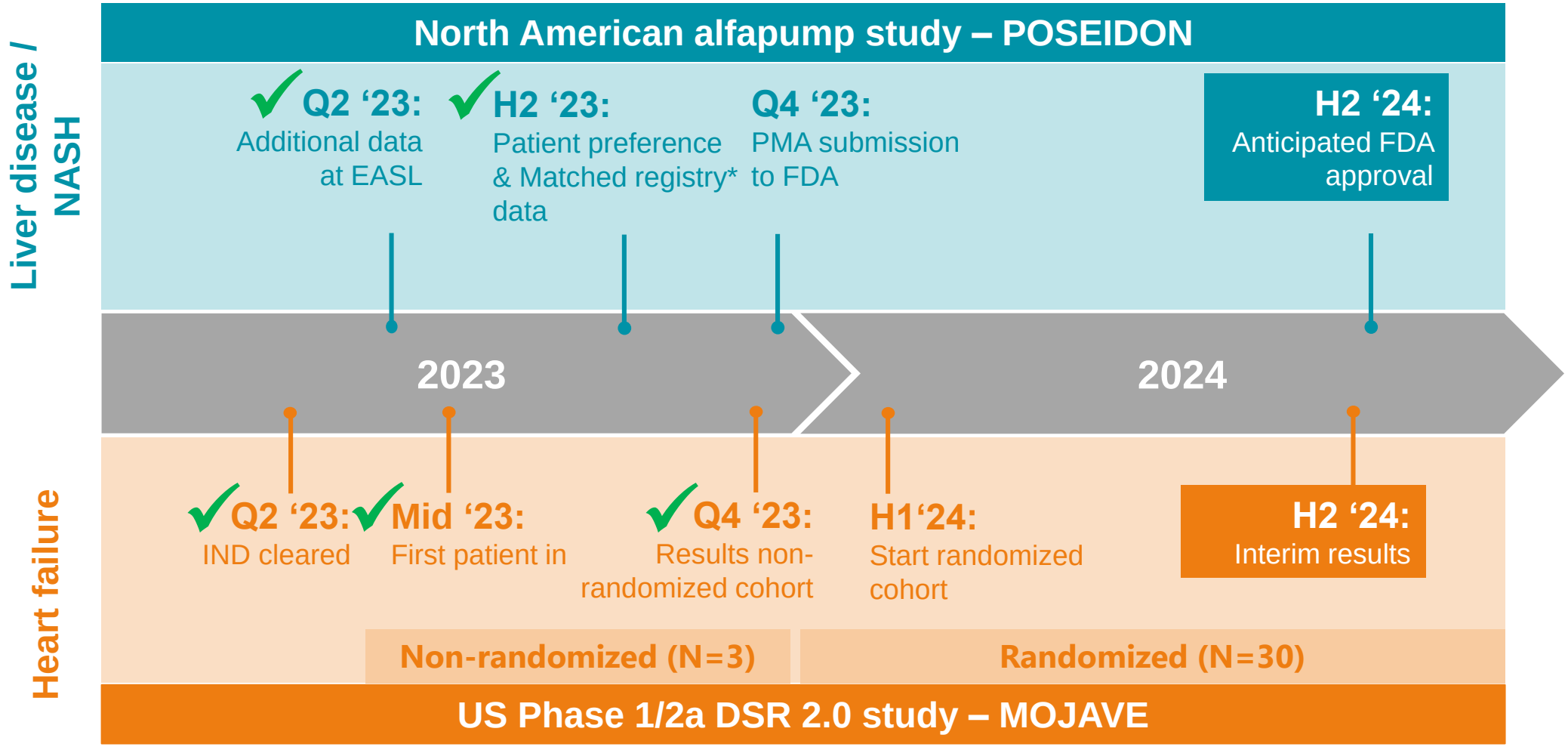
Strong outlook for key value drivers



** Data from propensity matched interim analysis of NACSELD (North American Consortium for the Study of End-stage Liver Disease) registry vs POSEIDON pivotal cohort*

Contact info

IR@sequanamedical.com

+32 498 053579

www.sequanamedical.com

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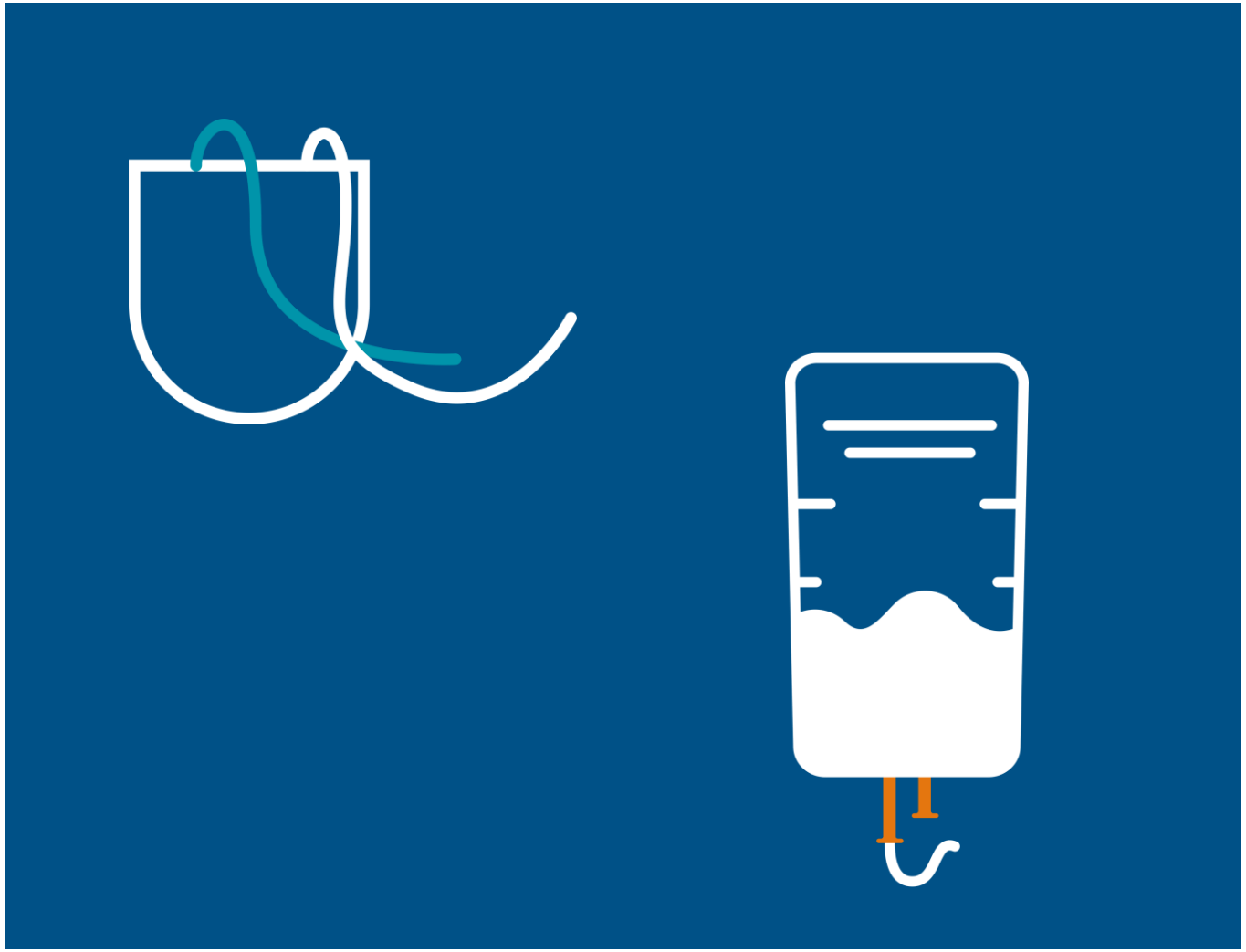


Back-up

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:

Ian 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

Rudy Dekeyser
Director

Wim Ottevaere
Director

Jackie Fielding
Director

Doug Kohrs
Director

Alex Clyde
Director

Kenneth Macleod
Director

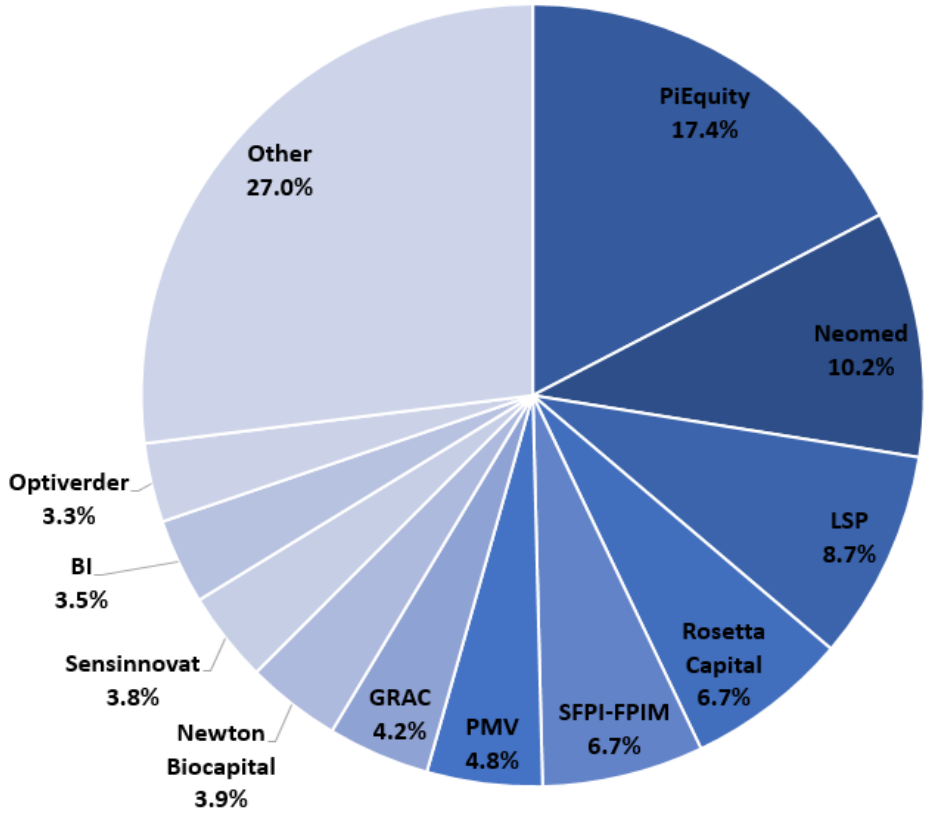
Ids van der Weij
Director

Ian Crosbie
Chief Executive Officer

Shareholders base and financial overview

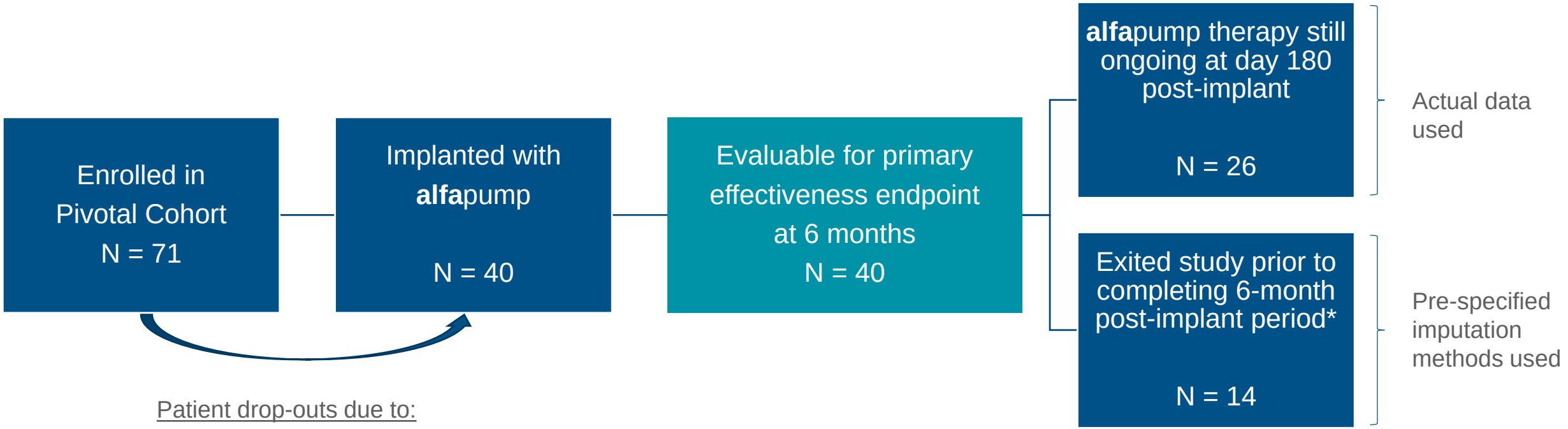
Ticker: SEQUA – Euronext Brussels

- Outstanding shares: 28.2M
- Outstanding shares corresponding to outstanding share options: 3.9M



- Analysts:
  - Degroof Petercam – Laura Roba
  - Edison – Pooya Hemami
  - H.C. Wainwright – Yi Chen
  - KBC Securities – Jacob Mekhael
  - Van Lanschot Kempen – Luísa Morgado
- Cash (30 June 2023): €17.1M
- Cash runway into Q1 2024

POSEIDON: Pivotal cohort



Patient drop-outs due to:
- COVID-19 related delays in elective surgery
- Not meeting inclusion criteria at time of implant decision

* Reasons for exiting study:
- death or withdrawal due to unrelated AE, liver transplant (N=8)
- **alfa**pump system, procedure or therapy related AE (N=6)

NASH: *Non-Alcoholic Steatohepatitis;* ***AE:*** *Adverse Event*

POSEIDON: Pivotal Data - Patient profile

40 severely decompensated patients – alcohol and NASH as key drivers of cirrhosis

Age (mean)	63.6 ± 9.5 yr
MELD score (mean ± SD)	15.2 ± 3.8
Cirrhosis etiology*	
- Alcohol	- 47.5%
- NASH	- 37.5%
- Viral hepatitis	- 12.5%
- Others	- 11.0%
TP per month prior to study (mean ± SD)	3.2 ± 1.5

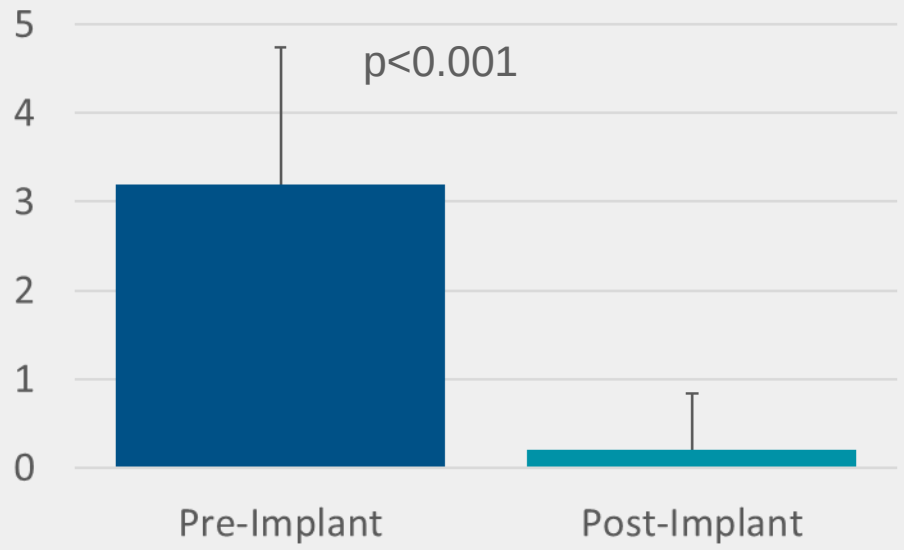
* *Some patients may have more than one etiology of cirrhosis*

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

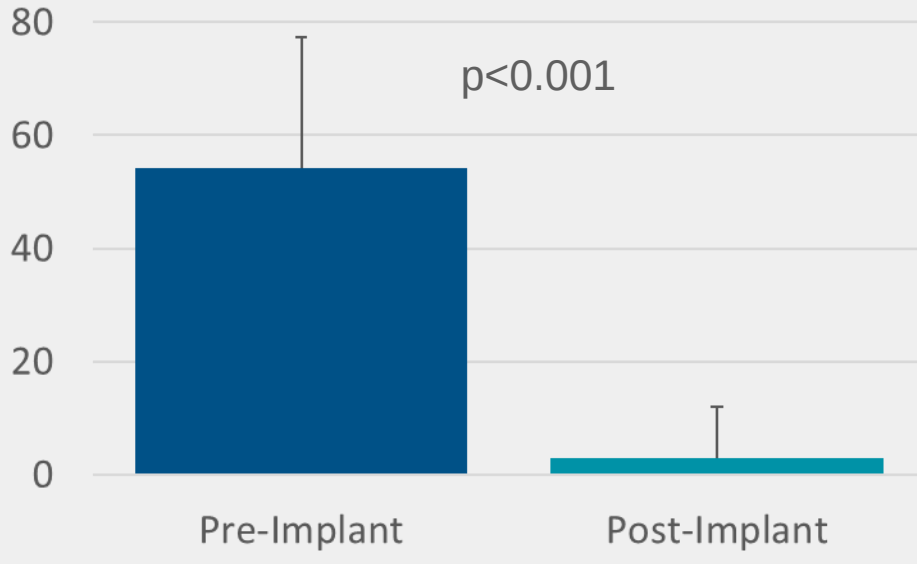
POSEIDON: Primary effectiveness endpoints exceed predefined thresholds for study success*

- **100%** median per-patient reduction in therapeutic paracentesis (p<0.001)**
  - *vs hypothesis of at least a 50% reduction*
- **77% of patients** with at least 50% reduction in therapeutic paracentesis (p<0.001)**
  - *vs hypothesis of at least 50% of patients*

Mean number of paracentesis per month:



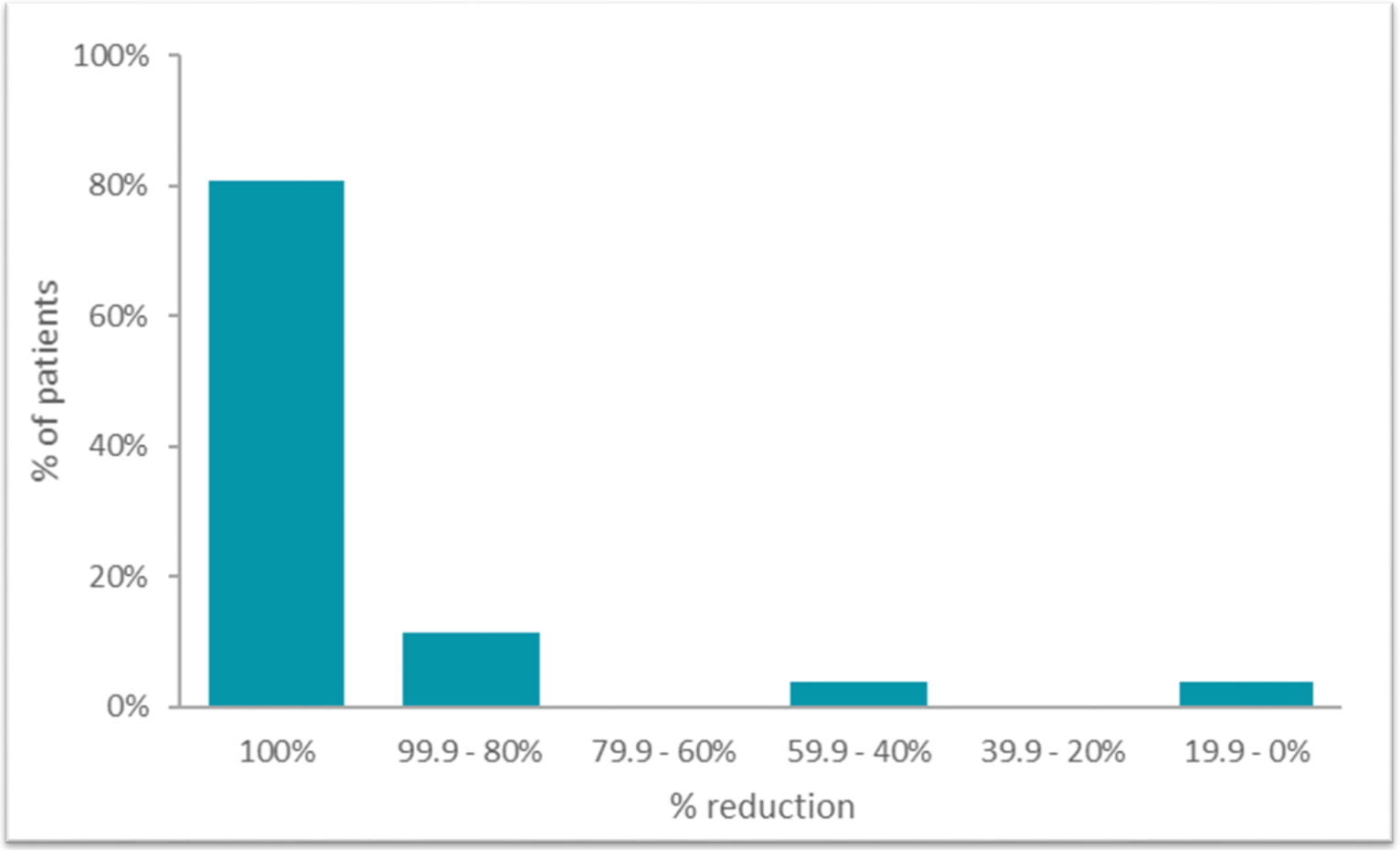
Cumulative ascites (L) drained by paracentesis:



* *As already reported in Press Release of 25 October 2022; ** Post vs pre-implant observation period*

POSEIDON: Observed data from patients completing alfapump therapy through day 180 post-implant*

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



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

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 – **alfa**pump 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

AE: *Adverse Event;* ***CEC:*** *Clinical Events Committee*

POSEIDON: Similar number of MAEs pre vs post implant

	3 months pre-implant (Day -90 to Day -1)		3 months post-implant (Day 91 to Day 180)	
	No. of events	No. of subjects with events	No. of events	No. of subjects with events
Major Adverse Events	**5**	3	**5**	4
AKI > stage 2	0	0	1	1
Hepatorenal Syndrome	0	0	1	1
Hepatic Encephalopathy > stage 2	4	2	1	1
Spontaneous Bacterial Peritonitis	1	1	1	1
Recurrent/Refractory Infection*	0	0	1	1

** Related to paracentesis or the **alfa**pump system, procedure or therapy*

Note: Secondary safety endpoint: Pivotal mITT population; events were adjudicated by the CEC; all implanted subjects in the Pivotal Cohort are included (N=40)

POSEIDON: Comparable number of serious infections pre vs post implant

	3 months pre-implant (Day -90 to Day -1)		3 months post-implant (Day 91 to Day 180)	
	No. of events	No. of subjects with events	No. of events	No. of subjects with events
All Serious Infections	**2**	2	**3**	3
Of which: **Ascites-Related Serious Infections**	**1**	1	**2***	2

** Of which 1 related to the **alfa**pump system*

Note: Secondary safety endpoint: Pivotal mITT population; events were adjudicated by the CEC; all implanted subjects in the Pivotal Cohort are included (N=40)

Despite AKIs, stable kidney function over long-term

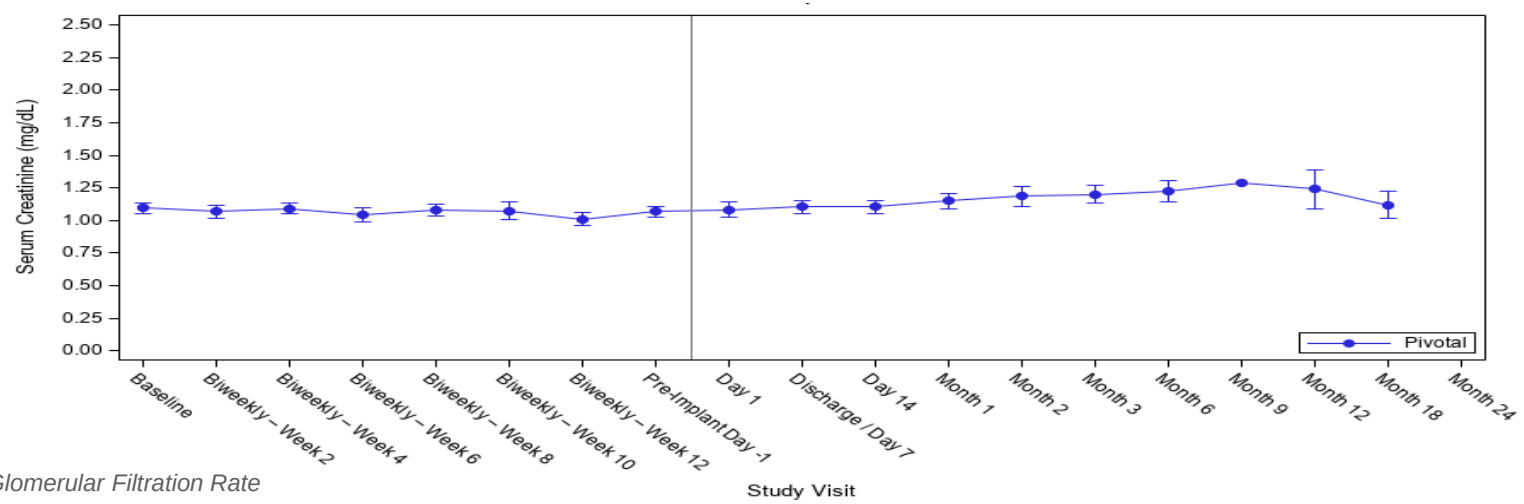
- **AKI events post-implant were manageable**

	6 months post-implant (Day 0 to Day 180)	
	No. of events	No. of subjects with events
AKI stage 1	16	14
AKI stage 2	4	4
AKI stage 3	2	2

AKI 1 of limited clinical relevance

AKI 2 and 3: three events resolved and three events were unresolved at the time of death from unrelated cause

- **Average serum creatinine (and eGFR) remained stable over time:**



eGFR: estimated Glomerular Filtration Rate

POSEIDON: QoL assessment

Two validated QoL methodologies are part of secondary endpoints

- SF-36:
  - General health-survey questionnaire
  - Endpoint: improvement* in SF-36 Physical Component Score
  - Subdomains of Physical Component Score: physical functioning, role physical, bodily pain, general health

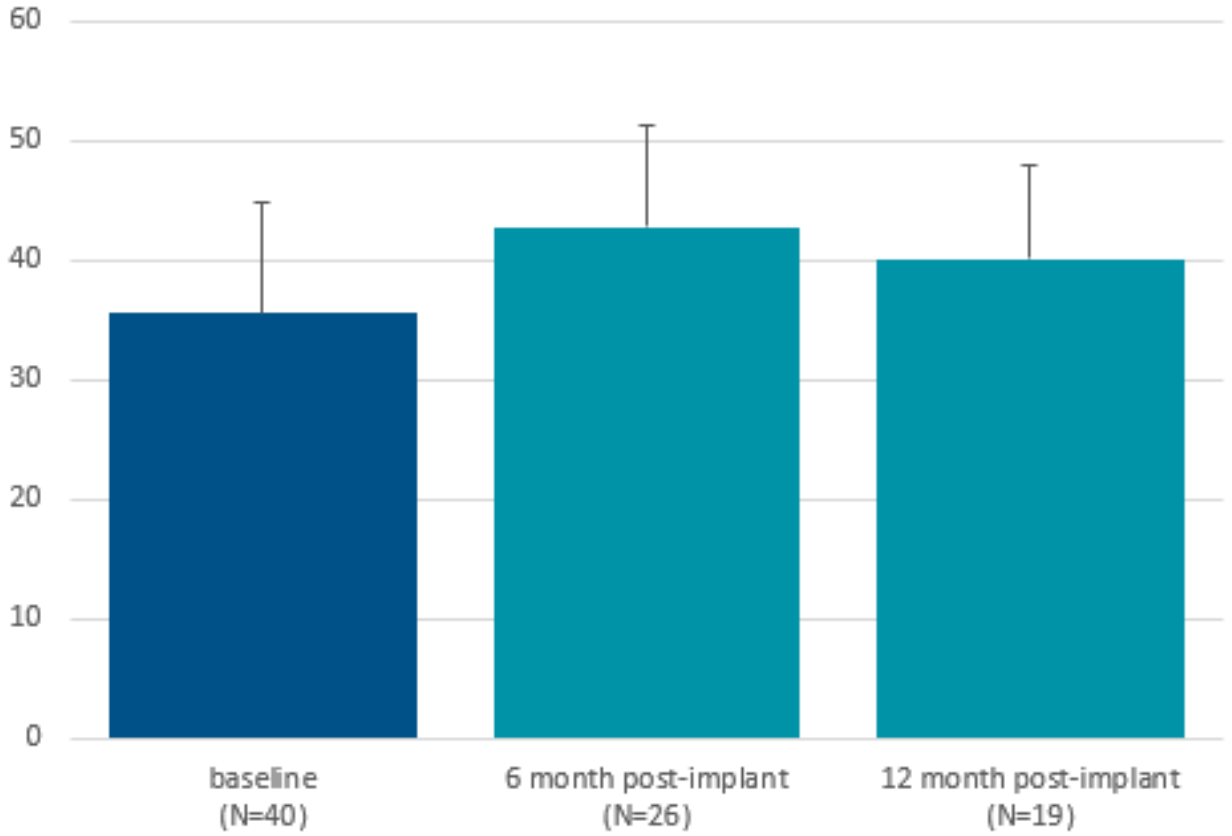
- Ascites Q:
  - Specific health-survey questionnaire for ascites
  - Endpoint: improvement* in Ascites-Q Score
  - Subdomains of Ascites-Q: abdominal fullness, lack of appetite, early satiety, nausea, abdominal pain, back pain, short of breath

QoL scores over time are compared to baseline, so do not reflect anticipated decline in QoL scores due to disease progression.

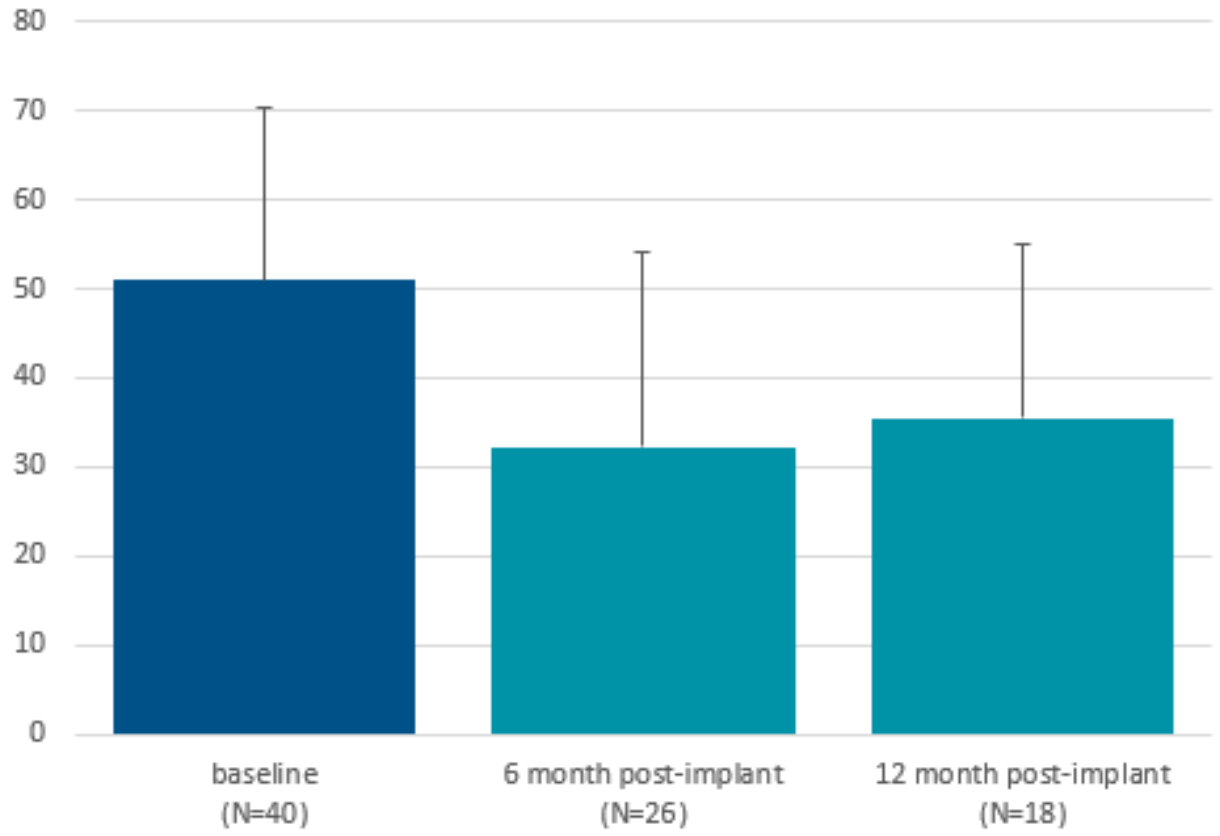
Therefore any reduction in QoL benefit over time may well be due to advancement of underlying disease rather than decline in alfapump benefit.

QoL: Maintaining clinically meaningful improvement despite disease progression

SF-36 Physical Component Score (higher is better):



Ascites Q Score (lower is better):



QoL: *Quality of Life*

SF-36 Physical Component Score is an independent predictor of mortality(1)

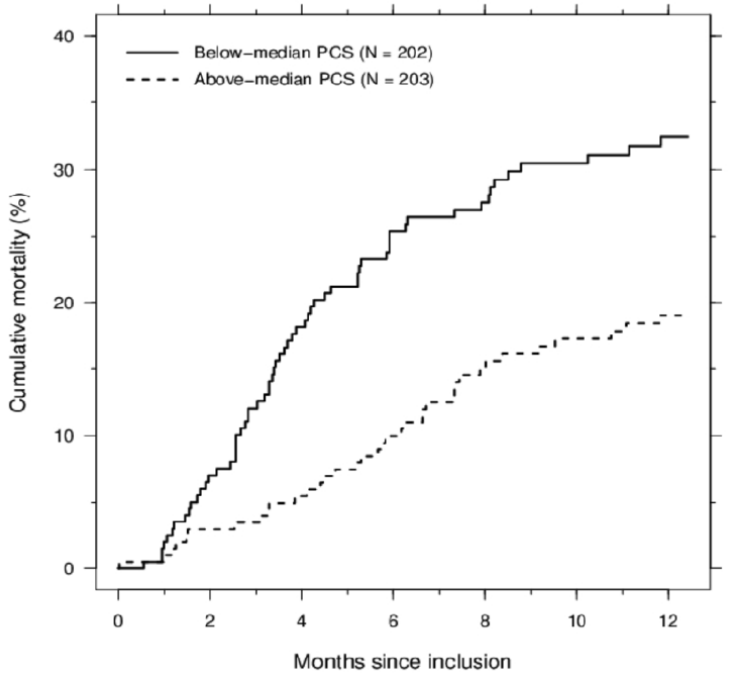
Multicenter randomized controlled study in patients with recurrent (N=164) and refractory (N=241) ascites

Patients stratified by survival 1 year after follow-up

Physical component score (range)	PCS of patients who died during follow-up	PCS of patients who survived follow-up	P-value
Physical component score	**34 (24-49)**	**41 (29-53)**	**0.01**
Physical function	45 (25-65)	50 (30-70)	0.42
Role Physical	0 (0-25)	0 (0-50)	0.05
Bodily pain	42 (22-80)	54 (41-74)	0.05
General health	35 (27-50)	40 (30-55)	0.12

- Patients that survived follow-up of 1 year were associated with higher median physical component scores

Cumulative all-cause mortality for patients below or above median physical component score (PCS)

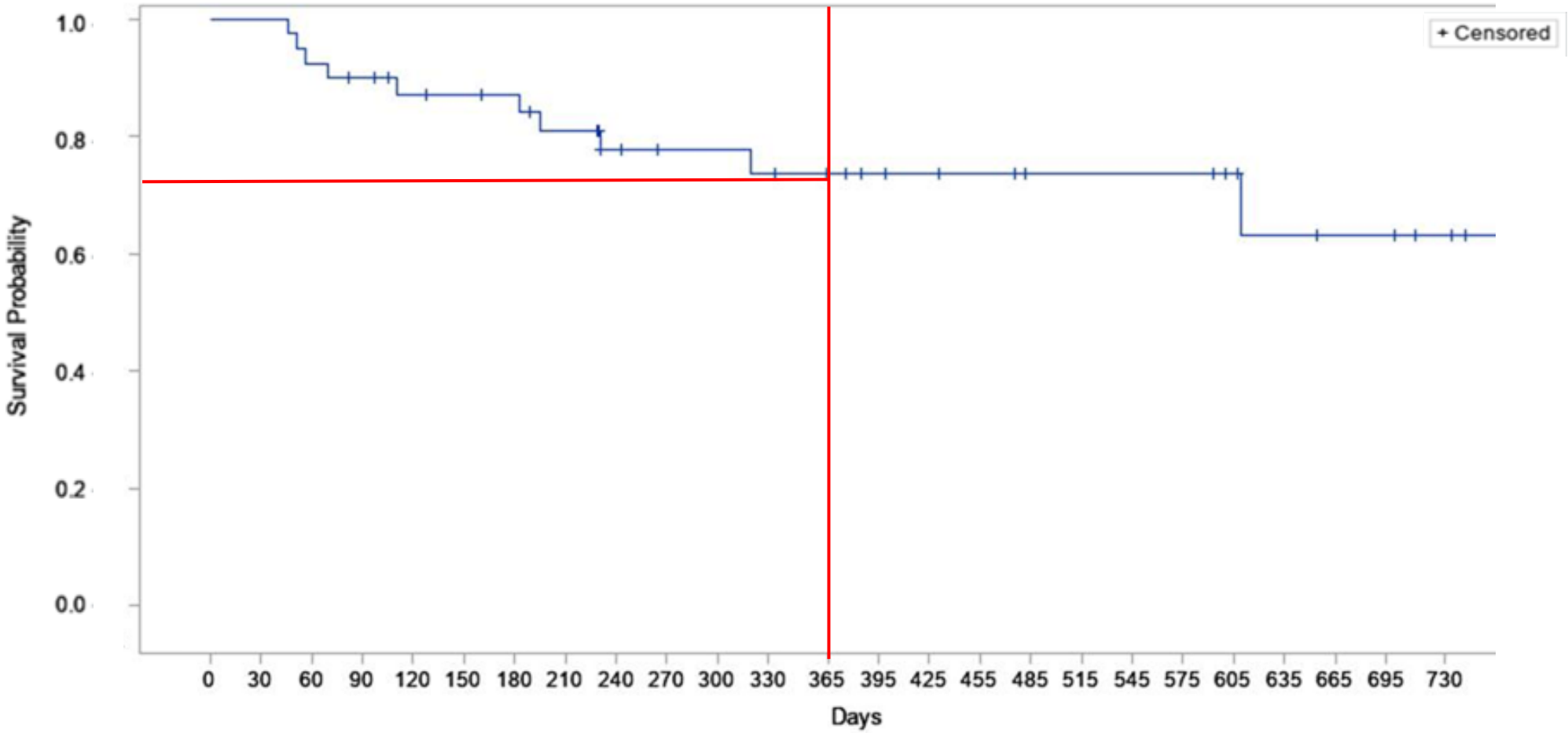


A higher physical component score in the SF-36 QoL tool predicted lower risk of death

Source 1: MacDonald and Jalan et al. – poster presentation at The International Liver Congress EASL 2018

Over 70% survival at 12 and 18 months post-implant

Compares favorably to literature citing only ~17% predicted survival at 12 months and ~5% at 18 months(1)



Note: POSEIDON study not powered for survival

Source 1: Salerno et al., Gastroenterology 2007; 133:825-834; predicted survival probability for refractory ascites patients with a MELD score of 15 and receiving paracentesis

Patient preference study completed

Recommended study by FDA to elicit patient preference for attributes of an implantable pump as a novel interventional treatment for ascites

- Rigorous study design pre-discussed with FDA:
  - Survey using discrete-choice experiment (DCE*) methodology conducted by RTI Health Solutions (thought leaders in the field)
  - 125 US patients with physician-confirmed recurrent or refractory ascites due to liver cirrhosis completed the survey
- Define risk for a treatment-related adverse event patients would be willing to accept (risk tolerance) to achieve specific improvements in treatment efficacy (desired benefits)
- Comparable patient profile to pivotal cohort in POSEIDON study

** The DCE approach allows an analysis of individual stated preferences in response to hypothetical choices and enables the quantification of the relative importance of each attribute/level during the decision-making process*

Study indicates profile exceeding patient expectations

Patient preference study indicates compelling profile for alfapump

Risk tolerance (over 6 months)	Patient preference study Maximum acceptable risk	POSEIDON pivotal cohort Observed rate
Major surgery or death	>10%	0%
Minor procedure	>35%	20%
Serious infection or AKI resulting in hospitalization	>30%	20%

Desired benefits	Patient preference study	POSEIDON pivotal cohort
Reduction in paracentesis frequency	100%	100% (median)
Additional ascites good health days each month	10	>10 (mean)

US patients are willing to tolerate risks beyond those observed for the alfapump in the POSEIDON study if the need for paracentesis is reduced

Data support hypothesis that alfapump is a desirable treatment option for the majority of patients

- ✓ Reduction in paracentesis frequency and additional ascites good health days are important attributes for a novel interventional treatment for ascites.

- ✓ Patients responded with a **65%** likelihood of selecting a treatment profile like the **alfa**pump vs regular paracentesis procedures and no implanted pump.

Patients have a strong preference for the alfapump vs continue their current paracentesis treatment

Matched cohorts: NACSELD registry vs POSEIDON

Comparing outcomes of POSEIDON pivotal cohort to matched patient group from NACSELD registry

- Consortium of tertiary-care hepatology centers in North America to study patients with cirrhosis
- NACSELD-III is an IRB-approved registry for outpatients with cirrhosis

Baseline values (mean)	NACSELD-III Registry Matched Patients (N = 40)	POSEIDON Pivotal Cohort (N = 40)
Ascites-Q Score	48	51
Sex (% male)	78%	65%
Age (yrs)	60	64
MELD-Na Score	16.3	15.2

NACSELD: *North American Consortium for the Study of End Stage Liver Disease;* ***IRB:*** *Institutional Review Board;* ***MELD:*** *Model for End-stage Liver Disease*

alfapump safety profile comparable to standard of care

Comparison for the six months post-implantation

Six month data[1]	NACSELD-III Registry Matched Patients	POSEIDON Pivotal Cohort[2]
Any Death or Hospitalization	**55.0% (22/40)**	55.0% (22/40)
Death	**12.5% (5/40)**	12.5% (5/40)
Hospitalization	**42.5% (17/40)**	42.5% (17/40)
Median # of hospitalizations (min, max)	**1 (0, 5)**	1 (0, 4)
Liver Transplant	**7.5% (3/40)**	5.0% (2/40)

Note: Additional data currently being analyzed for inclusion in PMA

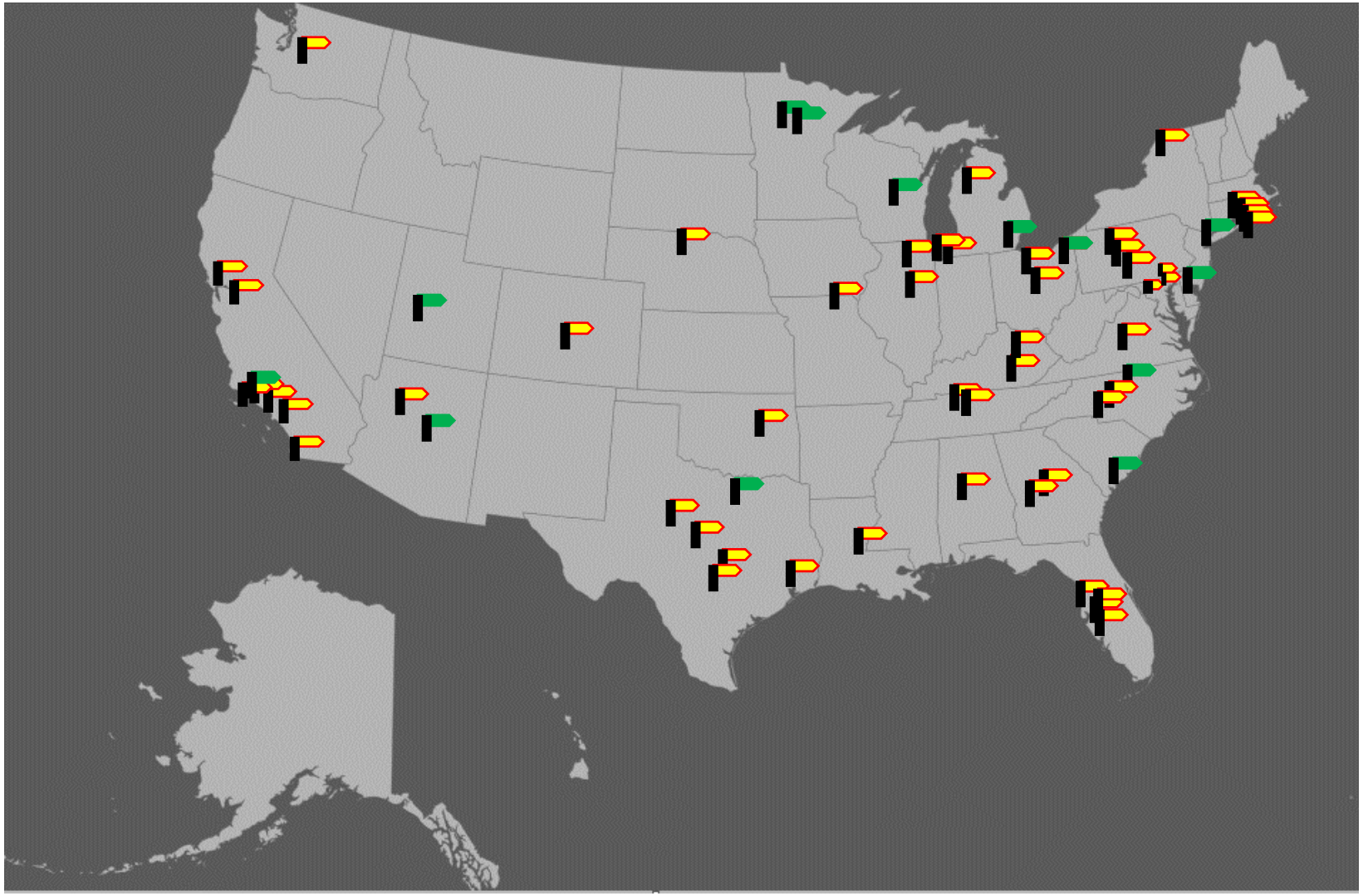
(1) Deaths and serious adverse events (SAE) requiring hospitalization are presented hierarchically such that if a subject died and experienced an SAE requiring hospitalization, they are counted under "Death".

(2) POSEIDON data are derived from adverse event data

Top 60 liver transplant centers (2021)

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

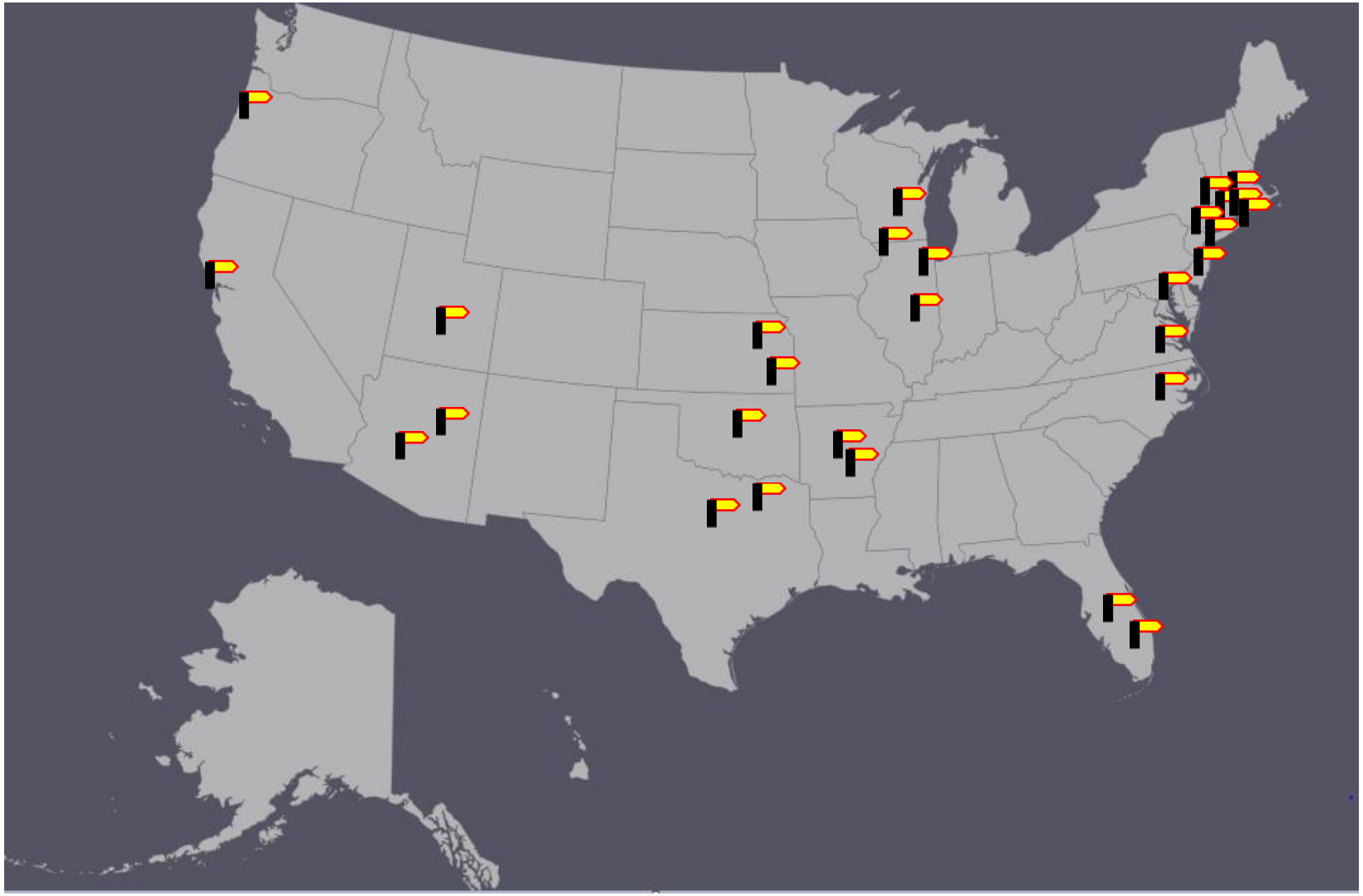
POSEIDON center (N = 13)



Source: Organ Procurement & Transplantation Network, US Dept of HHS (optn.transplant.hrsa.gov)

Top 61 – 90 liver transplant centers (2021)

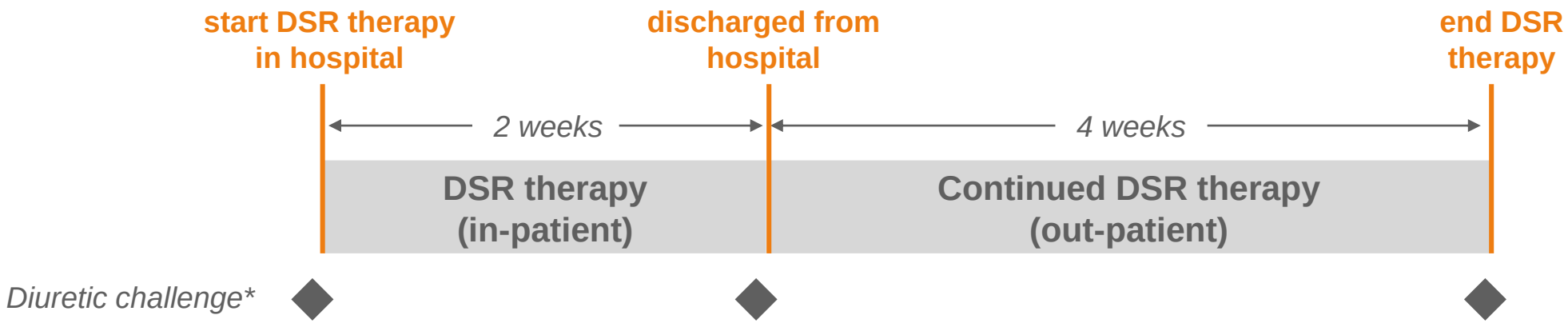
30 centers cover 15% of transplants (1,347 out of 8,685)



Source: Organ Procurement & Transplantation Network, US Dept of HHS (optn.transplant.hrsa.gov)

RED DESERT: First repeated DSR therapy study

Repeated dose proof-of-concept study of DSR in euvolemic 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 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

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

RED DESERT: 8 euvolemic heart failure patients

Severely ill heart failure patients on high doses of oral loop diuretics

	N=8
Ejection Fraction – % (Mean ± SD)	24 ± 3
NT-proBNP – pg/mL* (Mean ± SD)	4,589 ± 2,945
Furosemide equivalents – mg/day (Mean ± SD)	323 ± 263
Serum creatinine - µmol/L (Mean ± SD)	120 ± 53
eGFR - mL/min/1.73m^2 (Mean ± SD)	64 ± 23

** **NT-proBNP**: N-terminal-pro hormone B-type Natriuretic Peptide – analysed in local lab*

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

Presented as Late-Breaker and Highlight at Heart Failure 2021

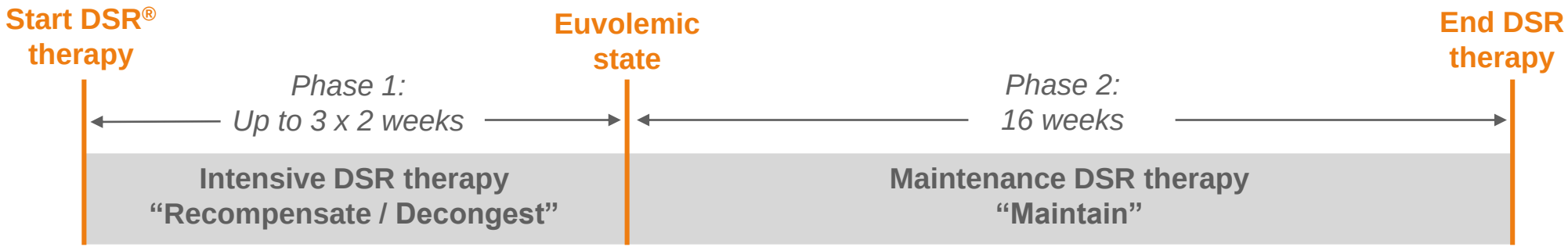
"Simultaneous normalization of diuretic response and improvement in cardio-renal status is a never before seen treatment effect" – Dr. Testani, Yale

** 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: Expansion into decompensated HF patients

Decompensated heart failure patients with persistent congestion on high dose diuretics



Study Endpoints

- **Primary:** safety and tolerability of DSR® therapy
- **Secondary:** feasibility of DSR therapy to restore and maintain euvolemia without additional loop diuretics

SAHARA: 10 heart failure patients with persistent congestion

	N=10
Ejection Fraction – % (Mean ± SD)	23 ± 4
NT-proBNP – pg/mL* (Mean ± SD)	6,628 ± 2,483
Furosemide equivalents – mg/day (Mean ± SD)	360 ± 197
Serum creatinine - µmol/L (Mean ± SD)	142 ± 46
eGFR – mL/min/1.73m^2 (Mean ± SD)	51 ± 23

***NT-proBNP**: N-terminal-pro hormone B-type Natriuretic Peptide*

SAHARA: Successful proof-of-concept study

10 evaluable diuretic-resistant HF patients with persistent congestion on 2-6 weeks of intensive DSR therapy[1]

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

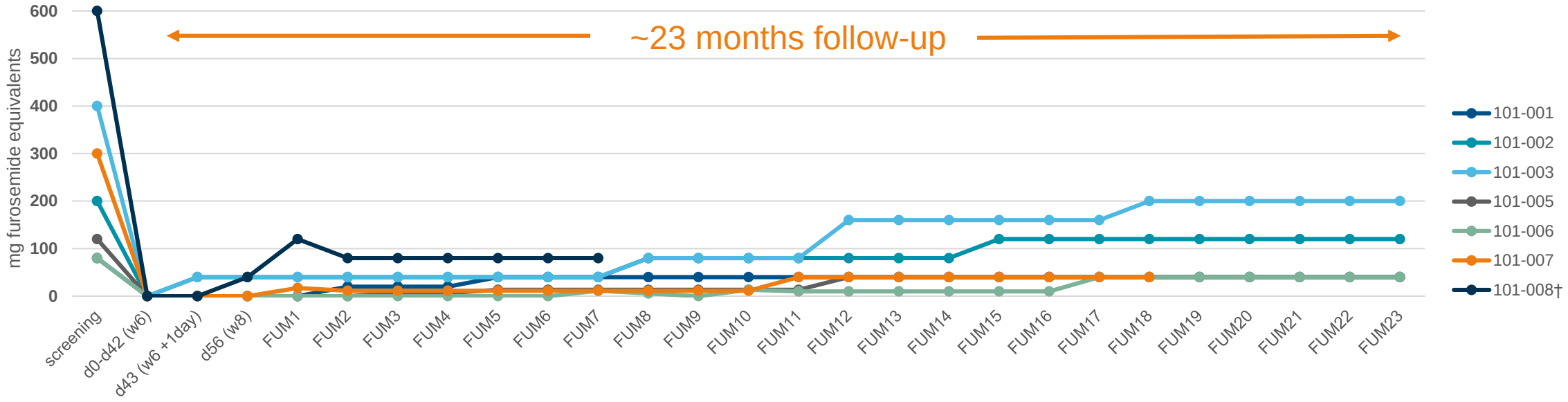
[1] *two additional patients were dosed but one patient died due to a cardiac arrest three days after study initiation and for one patient the study protocol was not correctly applied*

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*

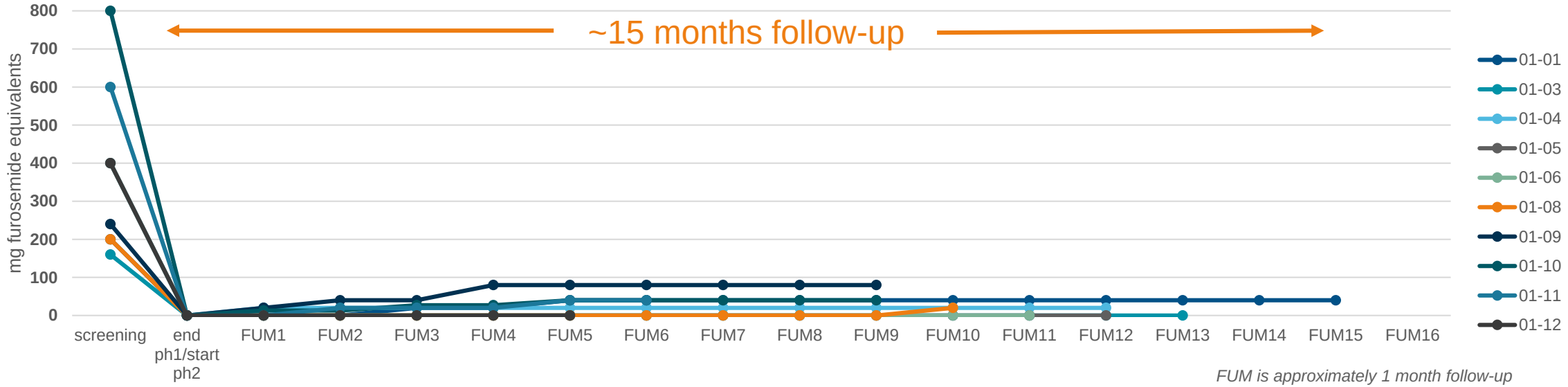
Long-term improvement in cardio-renal health

Durable and dramatic reduction in oral loop diuretic dosing as a result of improved disease status

RED DESERT



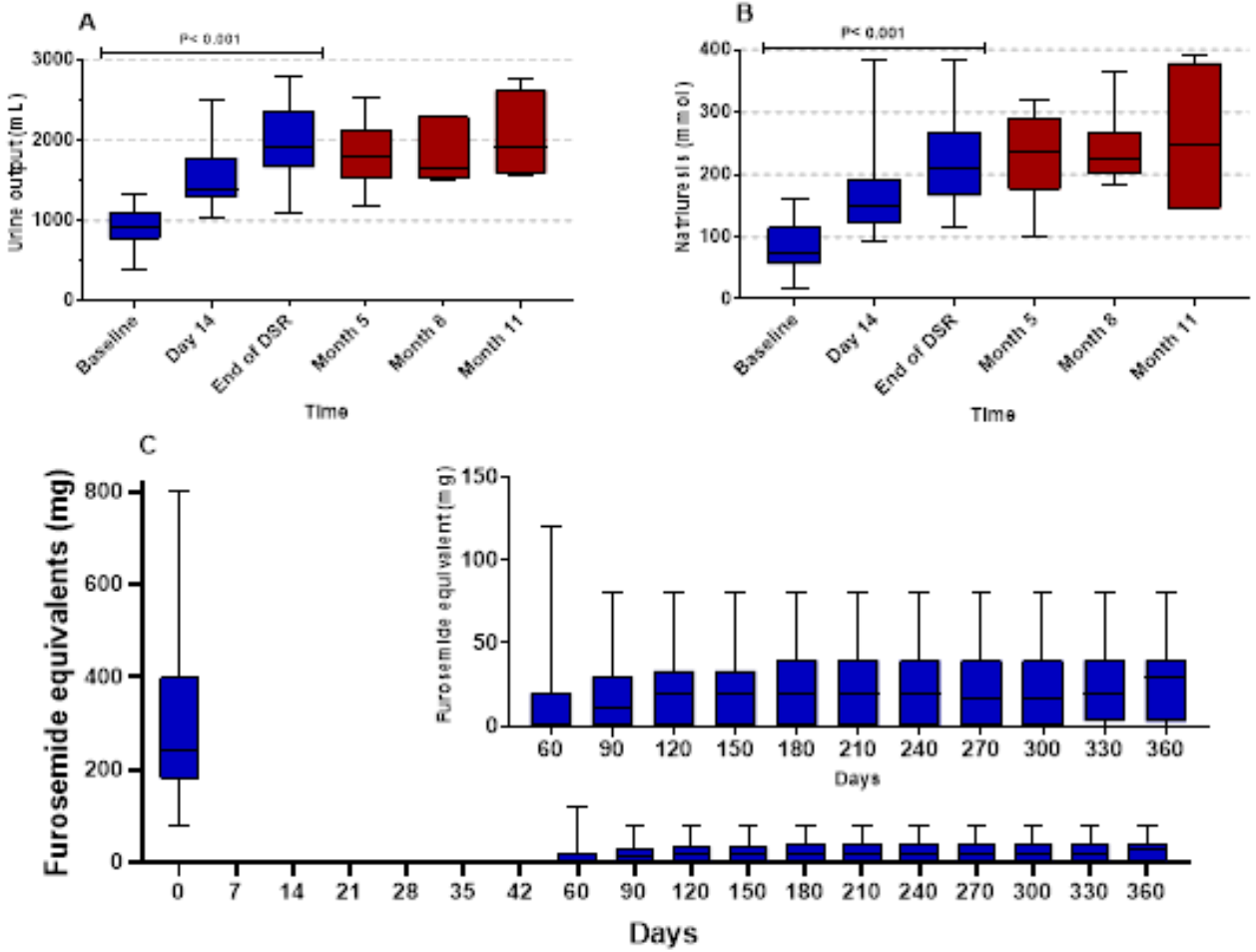
SAHARA



FUM is approximately 1 month follow-up

Improvement in diuretic response and LD dosing

Normalization of diuretic-response with dramatic durable reduction in LD needs post-DSR therapy



Cumulative 6-hour urine output and urinary sodium excretion following an intravenous 40mg dose of furosemide

Oral loop diuretic dose over the first year of follow-up

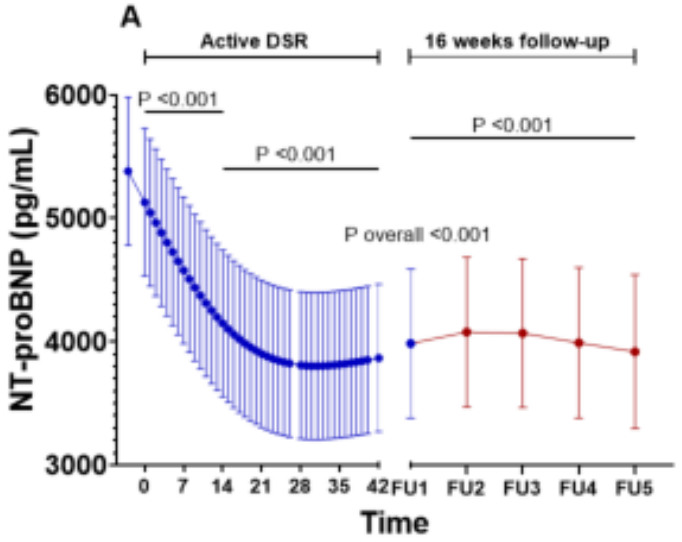
(in furosemide equivs: 1mg oral bumetanide = 20mg oral torsemide = 80mg oral furosemide)

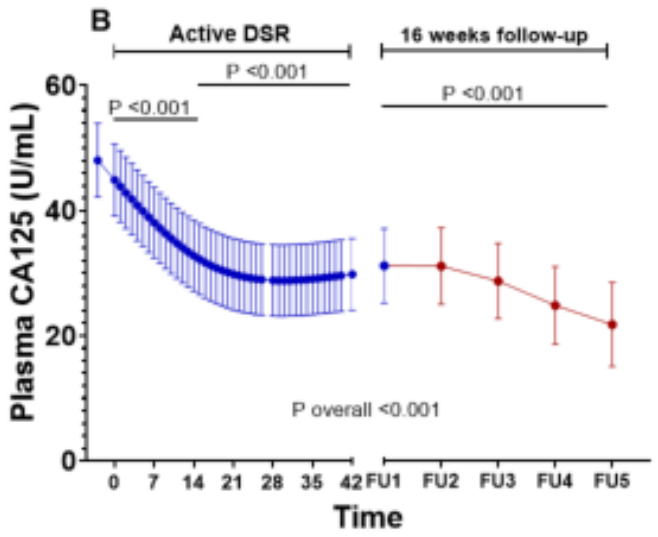
***Blue bars** indicate data from both RED DESERT and SAHARA, and **red bars** indicate data only from SAHARA.*

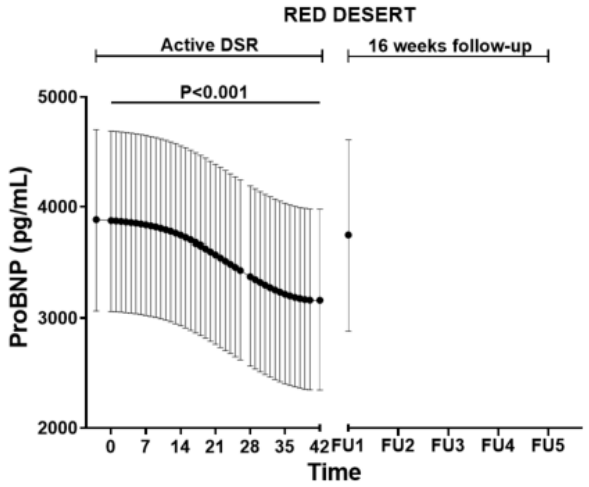
***LD**: Loop Diuretics*

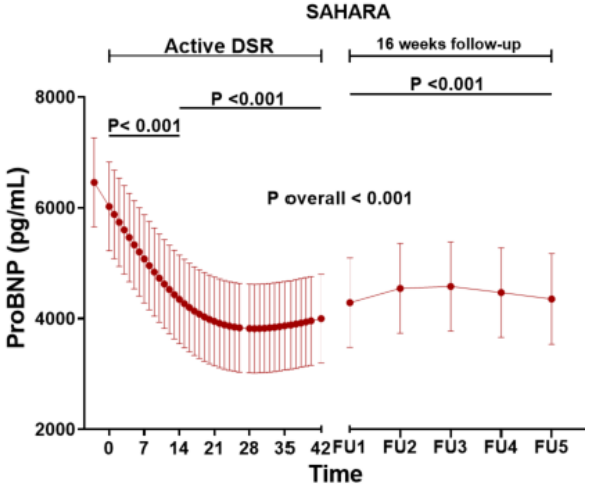
Significant improvement in volume status

All SAHARA patients reached euvolemia within seven days of DSR therapy (mean 7kg weight loss)









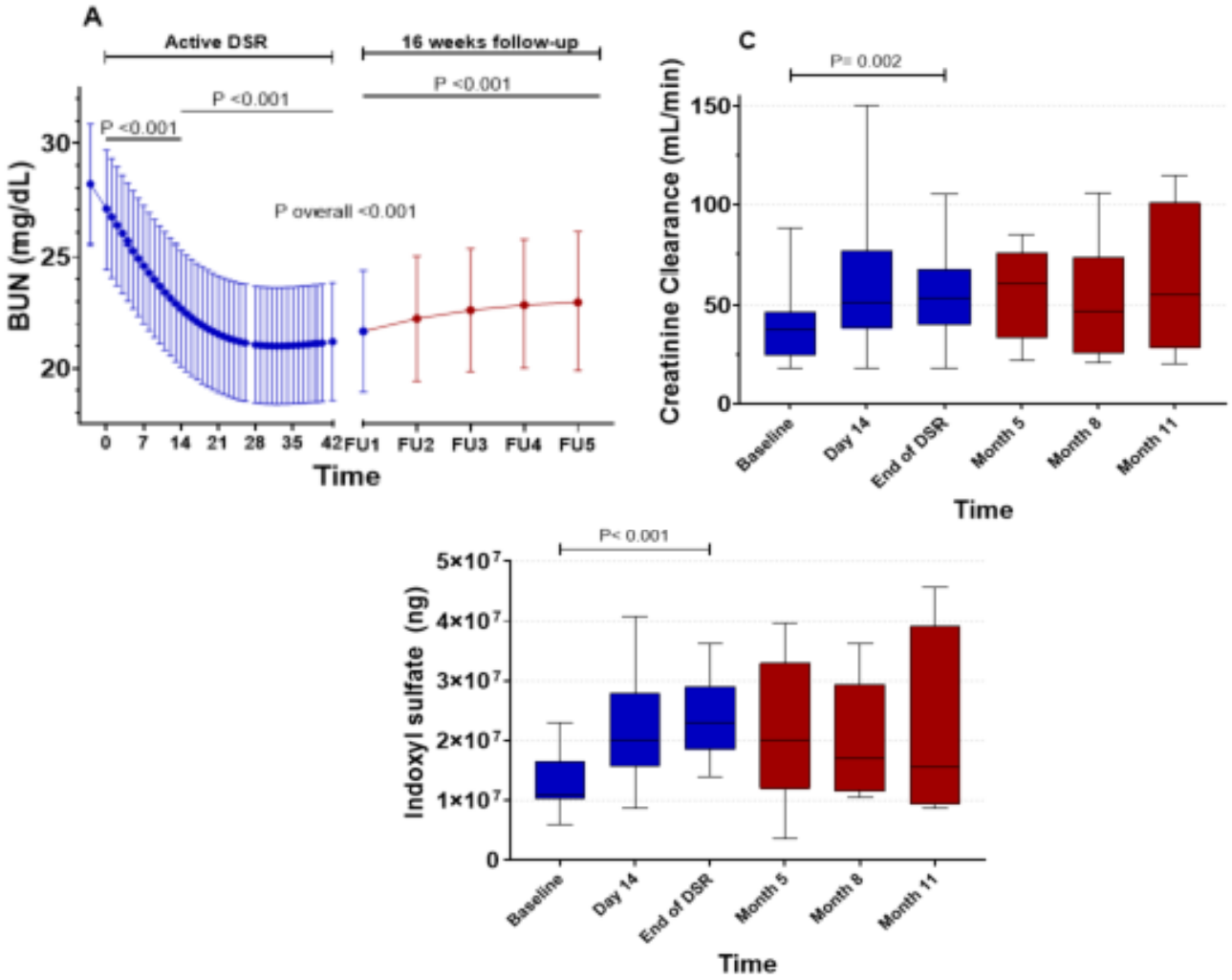
Change in NT-proBNP and Plasma CA125

Change in NT-proBNP for RED DESERT (euvolemic, stable HF) and SAHARA (hypervolemic decompensated HF)
Data are presented as *Mean (SEM)* over time.

Blue bars *indicate data from both RED DESERT and SAHARA, and* ***red bars*** *indicate data only from SAHARA.*

Broad improvement in kidney function

Removal of LD for extended period of time results in improved kidney health and function



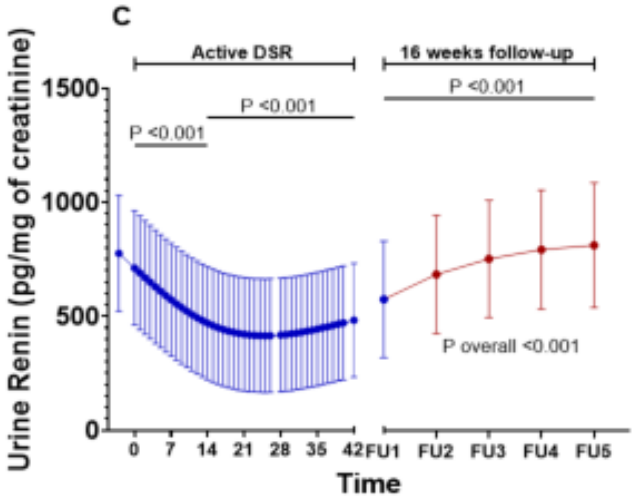
Blood urea nitrogen (BUN) and measured creatinine clearance

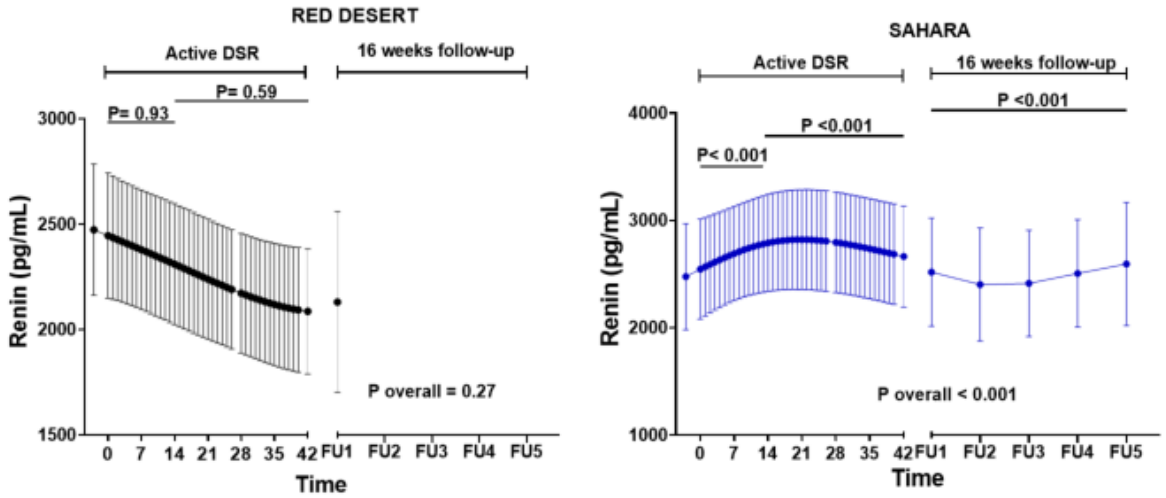
Cumulative 6-hour uremic toxin excretion - indoxyl sulfate

Blue bars *indicate data from both RED DESERT and SAHARA, and* ***red bars*** *indicate data only from SAHARA.*

DSR therapy impact on neurohormonal status

Managing volume status with DSR therapy appear to avoid the neurohormonal activation seen with LDs





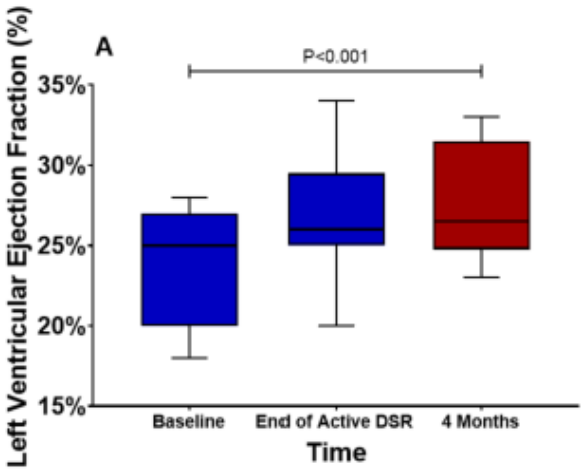
Urine renin – biomarker of local neurohormonal activation at the level of the kidney

Change in plasma renin for RED DESERT (euvolemic, stable HF) and SAHARA (hypervolemic decompensated HF)

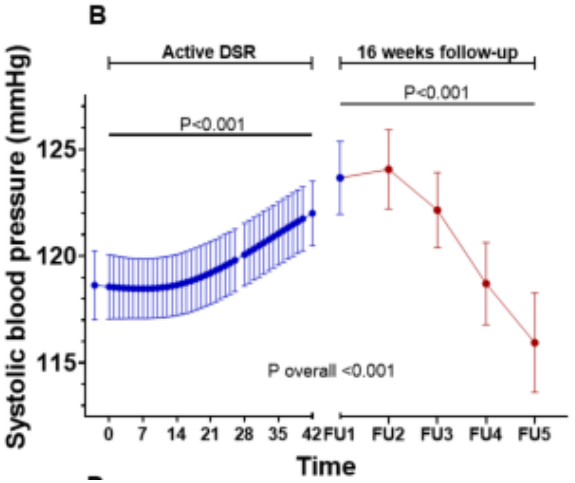
Data are presented as *Mean (SEM)* over time – active volume removal in SAHARA patients driving increase in renin

Blue bars *indicate data from both RED DESERT and SAHARA, and* ***red bars*** *indicate data only from SAHARA.*

Improvement in cardiovascular parameters



Improvement in LV ejection fraction

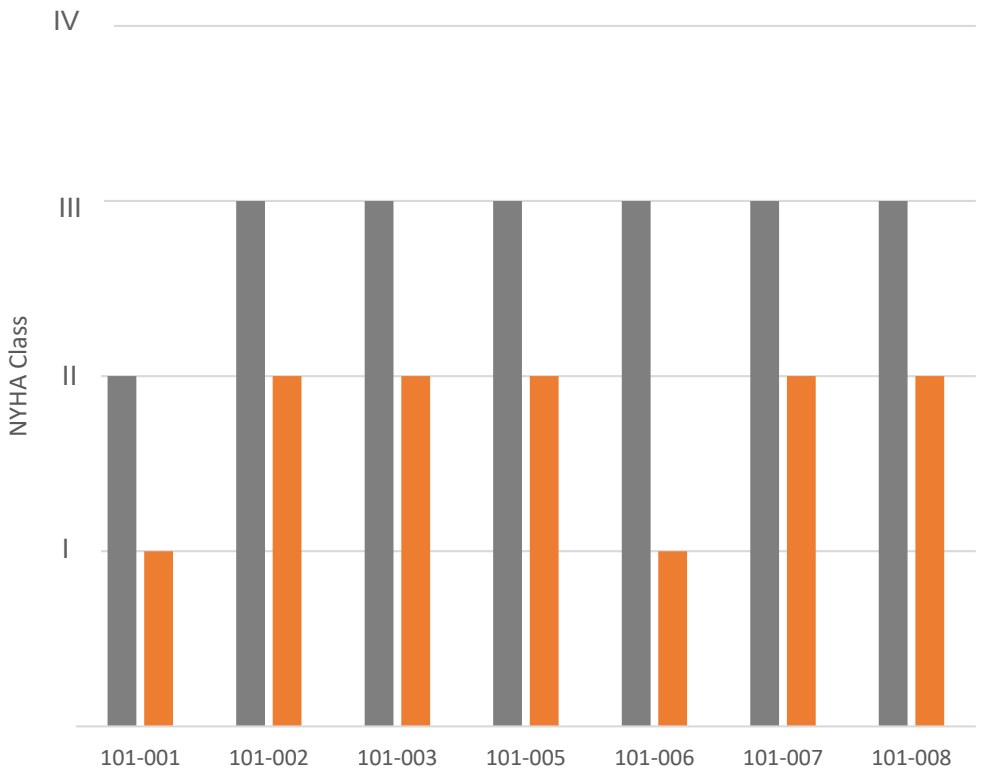


Change in systolic blood pressure – increase likely rules out any hawthorne impact in study from improvement in medication compliance

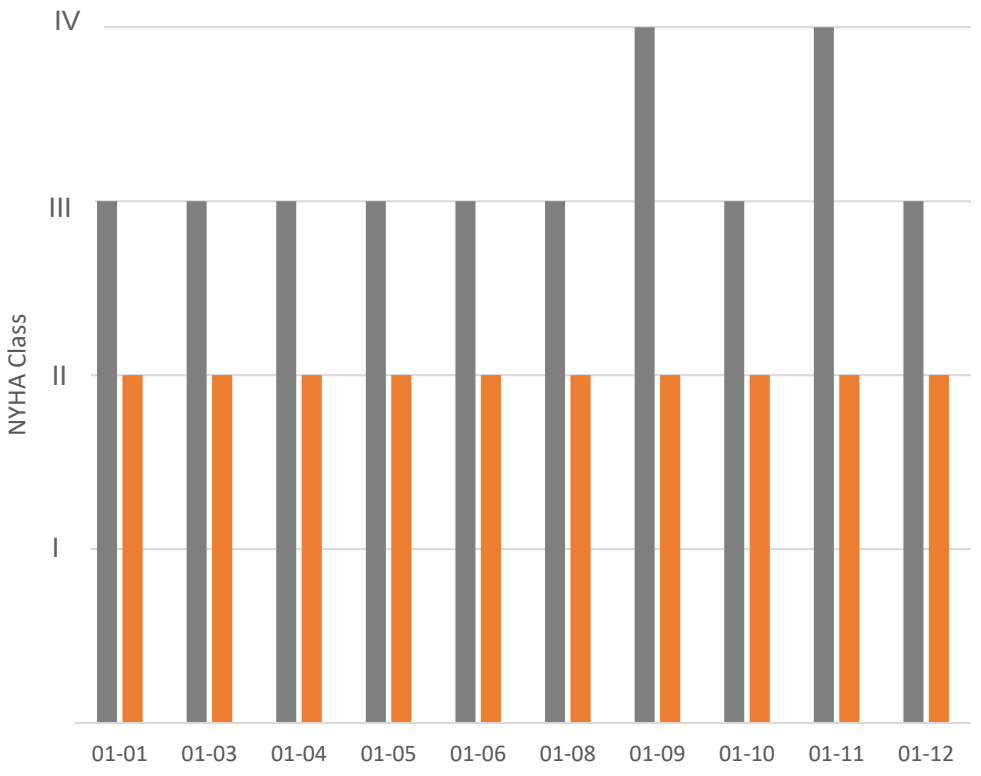
Blue bars *indicate data from both RED DESERT and SAHARA, and* ***red bars*** *indicate data only from SAHARA.*

Consistently improved NYHA class

RED DESERT



SAHARA



at screening
post DSR*

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

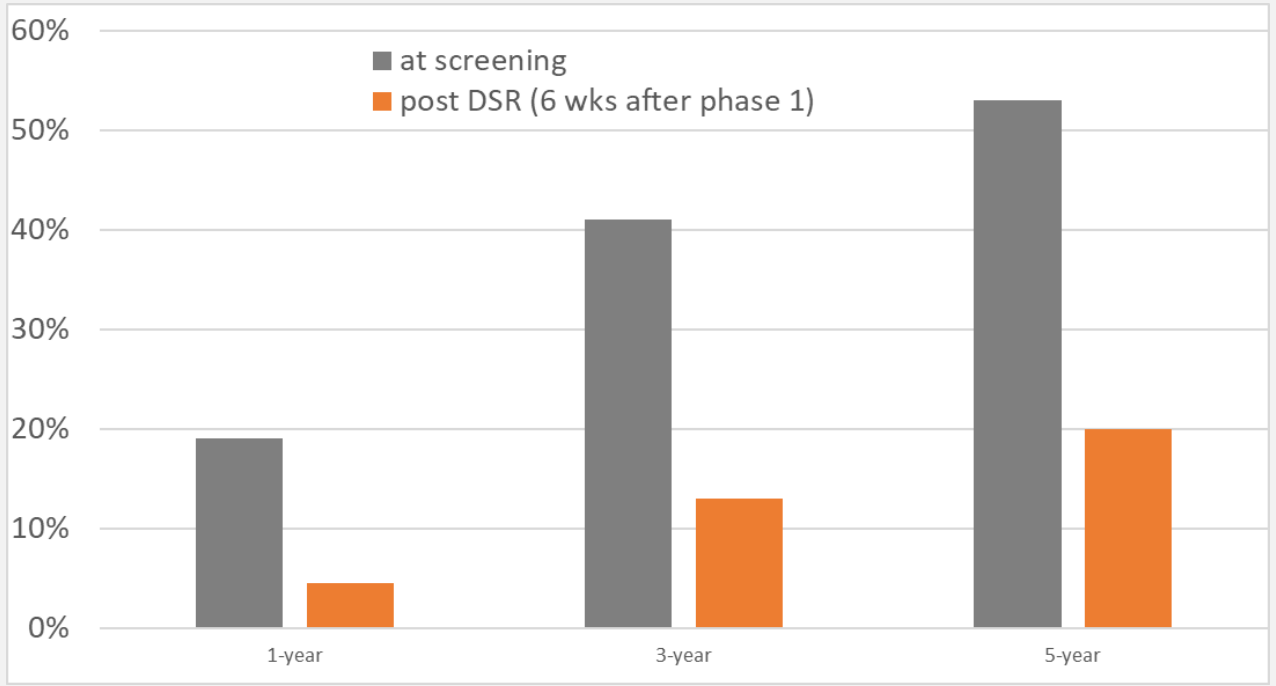
Note: data on NYHA classification collected outside study protocols of RED DESERT and SAHARA

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 = 6th week in RED DESERT; 2nd, 4th or 6th week in SAHARA)*

MOJAVE: Positive results from non-randomized cohort

US heart failure patients (N=3) with preserved ejection fraction (HFpEF) and severe diuretic resistance**

- All three US patients successfully treated with DSR 2.0
  - Maintenance of euvolemia without the need for any loop diuretics
  - No clinically relevant changes in serum sodium levels or progressive hyponatremia and no serious adverse events
  - Near normalization of diuretic response: + 324% in 6-hour urinary sodium excretion*
  - Broad improvement in kidney function: + 47% in eGFR* / - 57% in blood urea nitrogen*
  - Dramatic reduction in diuretic requirements up to 11 weeks after last DSR therapy:

Patient	No. of weeks after last DSR therapy	Reduction in furosemide equivalent dose vs. baseline
1	11.4	**97%**
2	6.4	**100%**
3	1.4	**100%**

DSR 2.0 is safe and well tolerated, restores diuretic response and improves cardiorenal status

** Mean values after 4-week DSR therapy vs baseline*

*** average furosemide equivalent dose of 1,227 mg per day*

DSR 2.0 improves therapeutic and safety profile

Strong granted IP drives high margin recurring revenue stream

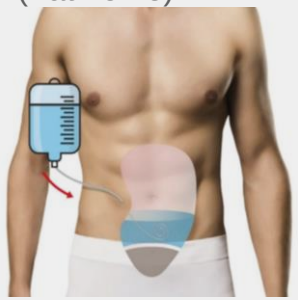
DSR 1.0 Sodium-free D10% (off-the-shelf)	DSR 2.0 Sodium-free dextrose / icodextrin (proprietary)
✓ Clinical proof-of-concept ✓ Rapid clinical path ~ Therapeutic profile / Ease of use ~ Safety profile	✓ Improved therapeutic profile ✓ Favorable safety profile ✓ Strong granted IP position in US & Europe • "Low or no sodium drug for the treatment of heart failure" • Drives recurring revenue from high gross margin consumable
✓ RED DESERT ✓ SAHARA	✓ CHIHUAHUA – MOJAVE

DSR Delivery – Low risk innovation drives convenience

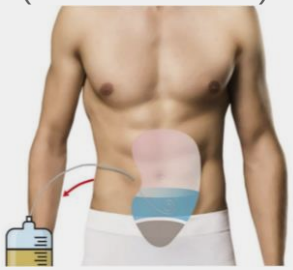
4-week DSR therapy with decreasing frequency / ~30 minutes at doctor's office or infusion center

TODAY
PD catheter

Fill
- doctor's office
- infusion center
(- at home)



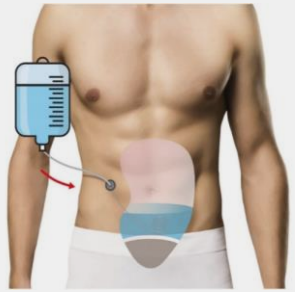
Drain
- at home
(- doctor's office)
(- infusion center)



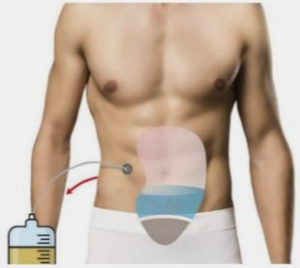
- Simplest approach
- "Drug only" approval pathway
- Hygiene concern & delay in therapy start
- Long term implantation is challenging

NEXT
Subcutaneous Port

Fill
- doctor's office
- infusion center



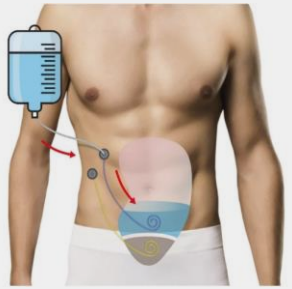
Drain
- at home
(- doctors office)
(- infusion center)



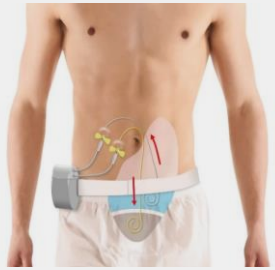
- Improved convenience and "image"
- No hygiene concerns, no therapy delay
- 510(k) approval pathway for port
- Ports can be left in body for next time

FUTURE VISION
Port and Pump

Fill + attach pump
- doctor's office
- infusion center



Drain
- everywhere
- anytime



- Internal or external pump
- Drain to bladder or external
- Highest patient convenience
- Permits tailored drain profile

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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 by delaying initialization of cost and burdensome hemodialysis
  - ⇨ 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 hospitalizations, the cost and burden of hemodialysis therapy as well as mortality

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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

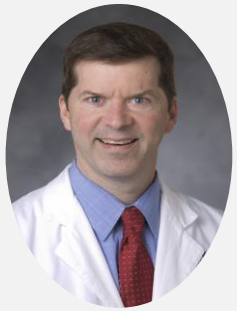
Professor of Medicine at Cleveland Clinic Lerner College of Medicine at Case Western Reserve University

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