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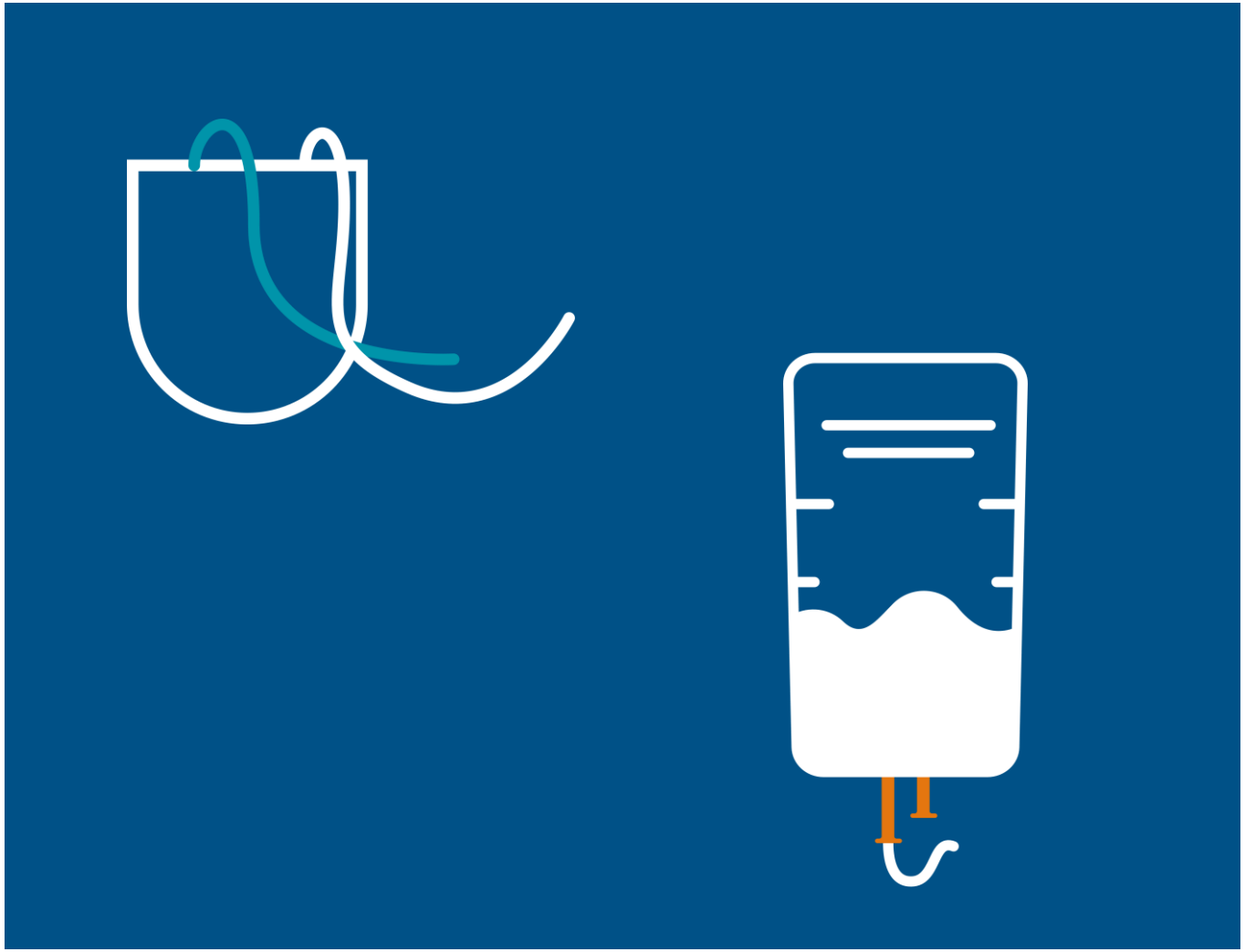

Additional data strengthens alfapump & DSR product profiles

alfapump: 12 month follow-up, matched registry analysis and patient preference study

DSR: First two MOJAVE patients and mechanism of action

Webcast presentation – 19 October 2023

Today's presenters

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- 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.

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Note:

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

Strong data reported in both programs

Further strengthening of alfapump PMA submission and encouraging early data from DSR MOJAVE study

alfapump® – strong positioning & US approval in liver disease expected in 2024

- ✓ One-year **alfa**pump data from POSEIDON shows **safety and strong efficacy profile is maintained at 12 months**
- ✓ Patient preference study indicates that US patients have a **strong preference for the alfapump** vs large volume paracentesis
- ✓ Matched interim analysis of patients from NACSELD registry and POSEIDON pivotal cohort indicates **alfapump safety profile is comparable to standard of care**
- ✓ **Positive pre-PMA meeting held with FDA** to align on clinical data and benefit-risk analysis for submission package
- ✓ On track for **PMA submission by year end**

DSR® – MOJAVE on track; DSR breaking vicious cycle of cardiorenal syndrome

- ✓ **First two US patients** from non-randomized MOJAVE cohort **successfully treated with DSR 2.0**
- ✓ Initial data indicate that DSR 2.0 is **safe and well tolerated, restores diuretic response and improves cardiorenal status**
- ✓ Biomarker analysis from RED DESERT and SAHARA studies supports **DSR's mechanism of action as breaking vicious cycle of cardiorenal syndrome**
- ✓ **Start of randomized MOJAVE cohort** of up to 30 US patients planned for **Q1 2024** following DSMB review

PMA: *Pre-Market Approval;* ***NACSELD:*** *North American Consortium for the Study of End Stage Liver Disease*

alfapump®

Proven step change in the treatment of liver refractory ascites

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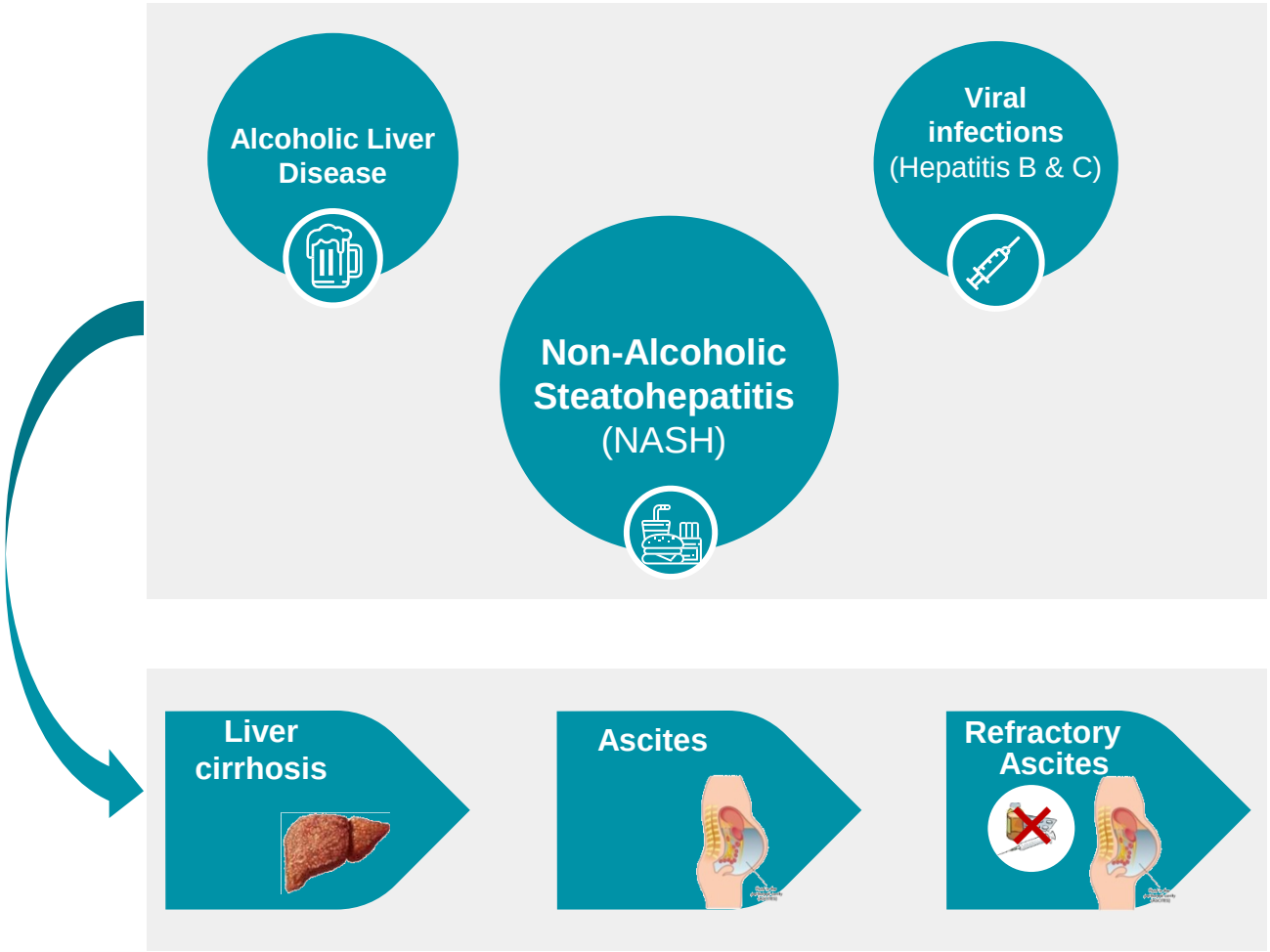
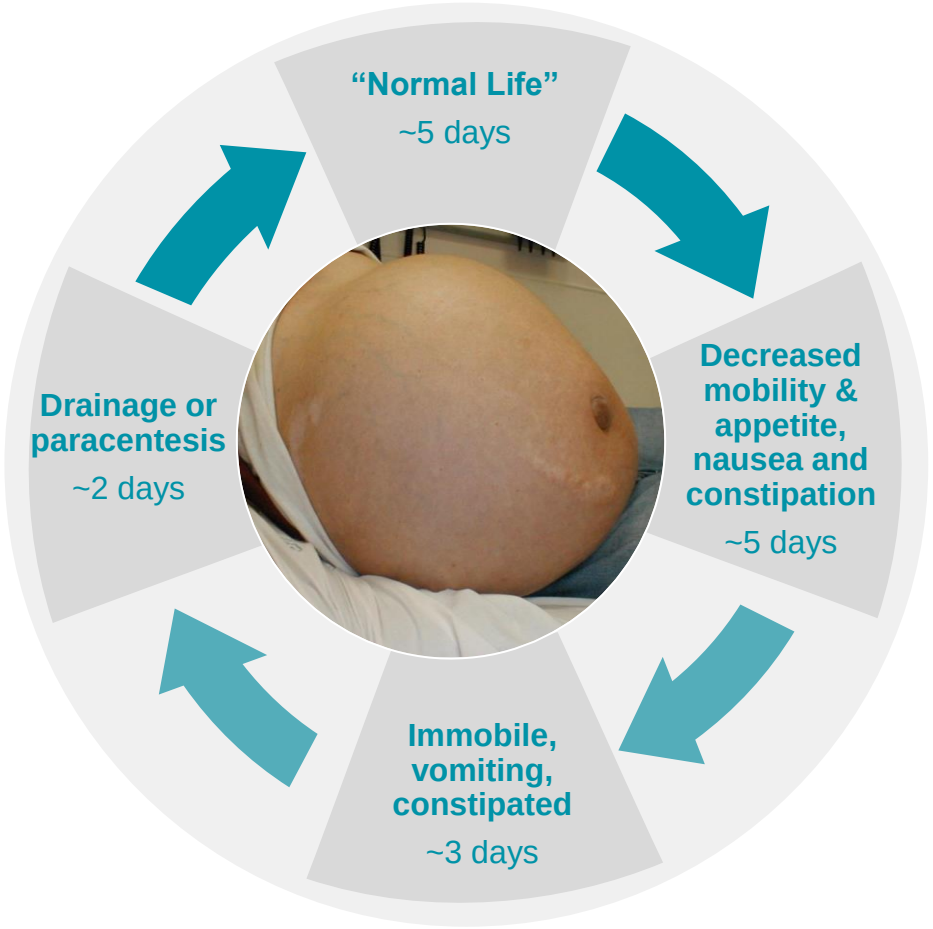
Refractory ascites – key complication of liver cirrhosis

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



Typical patient life[1]

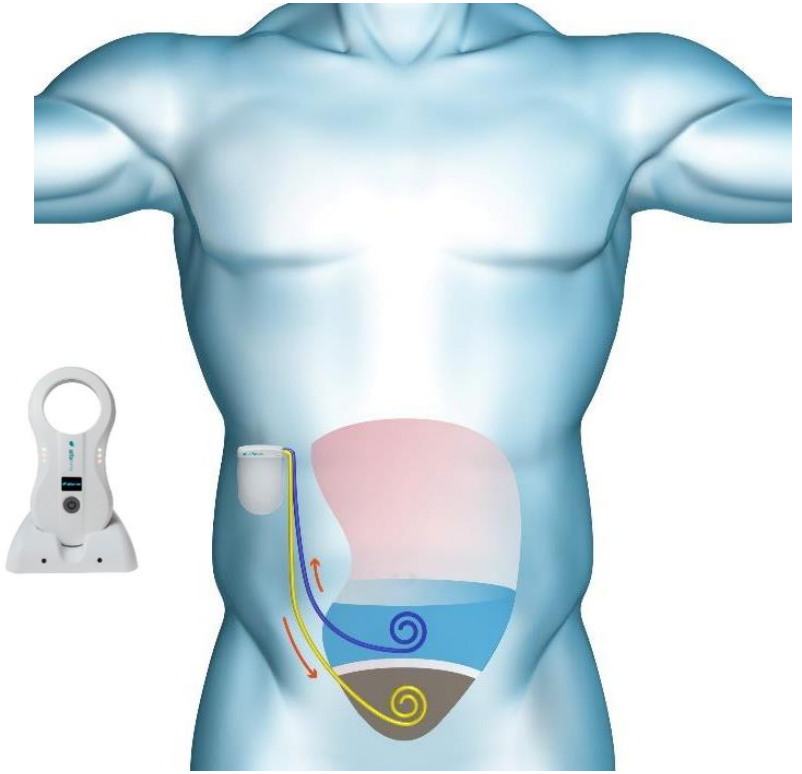


Source 1: Presentation of Dr. Rajiv Jalan at EASL in 2018, Large Volume Paracentesis (LVP) treatment cycle for refractory ascites

alfapump – continuous ascites removal to the bladder

Fully implanted automatic device for long term implantation

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



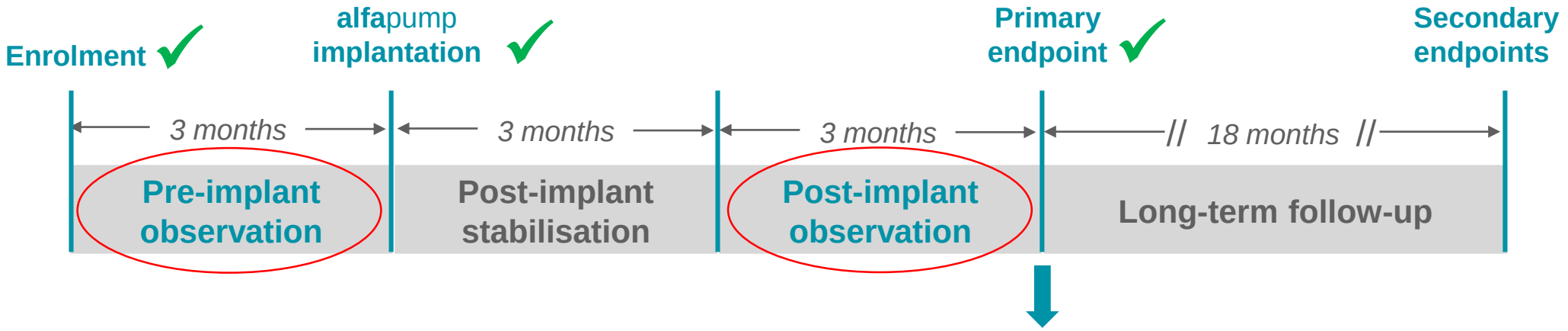
Breakthrough Device Designation

Over 1,000 systems implanted

Strong IP barriers through extensive patent portfolio & know-how

POSEIDON – Successful North American pivotal study

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



All primary endpoints met at 6-month post-implant ***(reported on 25 October 2022)***

- **Primary effectiveness endpoint exceed predefined thresholds for study success**
  - **100%** median per-patient reduction in therapeutic paracentesis (p<0.001)* *vs at least 50%*
  - **77% of patients** with at least 50% reduction in therapeutic paracentesis (p<0.001)* *vs at least 50%*
- **Primary safety endpoint data in line with expectations**
  - No unanticipated adverse device effects
  - 6 primary safety events

** Post vs Pre-implant observation period*

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

✓ Strong efficacy of alfapump maintained

- 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) over 6 month period**
- Number of major adverse events and serious infections in line with expectations
- Stable kidney function up to 12 months post-implant

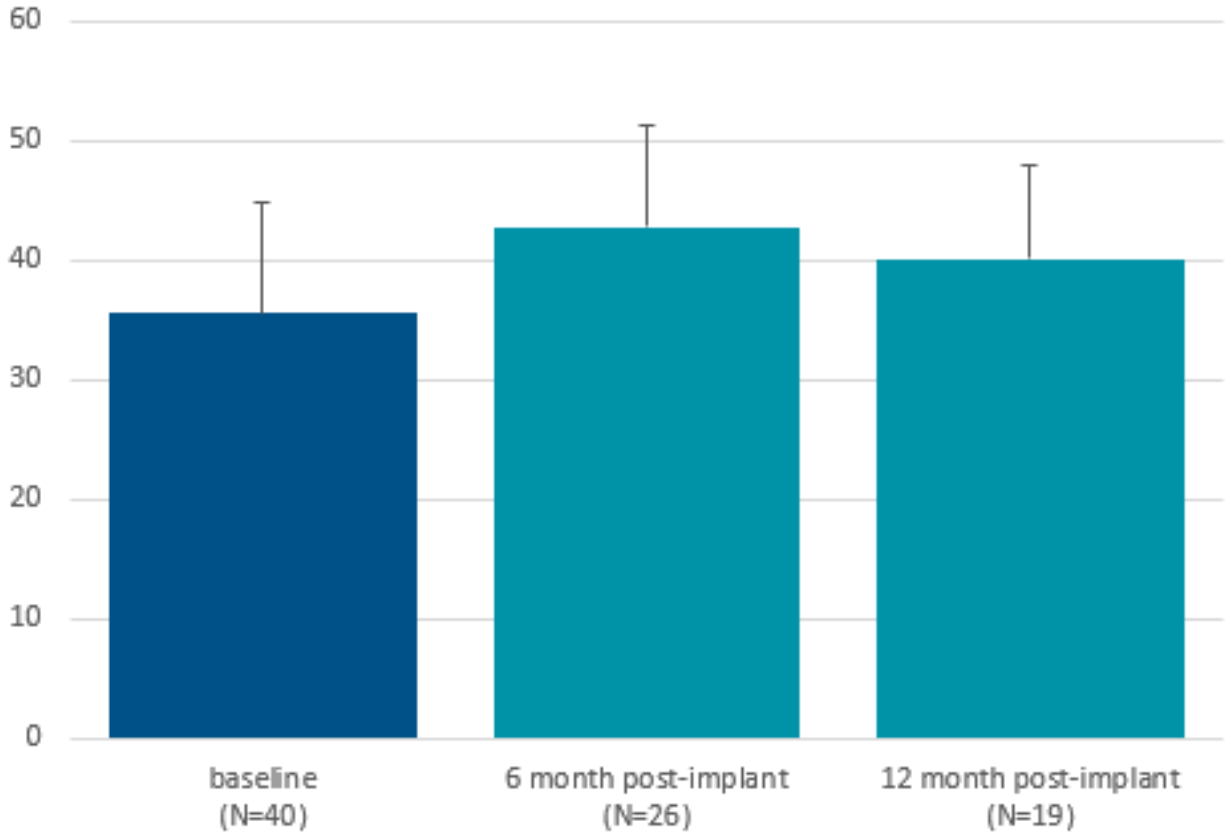
** 7-12 month post-implant period vs 3 month pre-implant observation period*

*** during 7-12 month post-implant period*

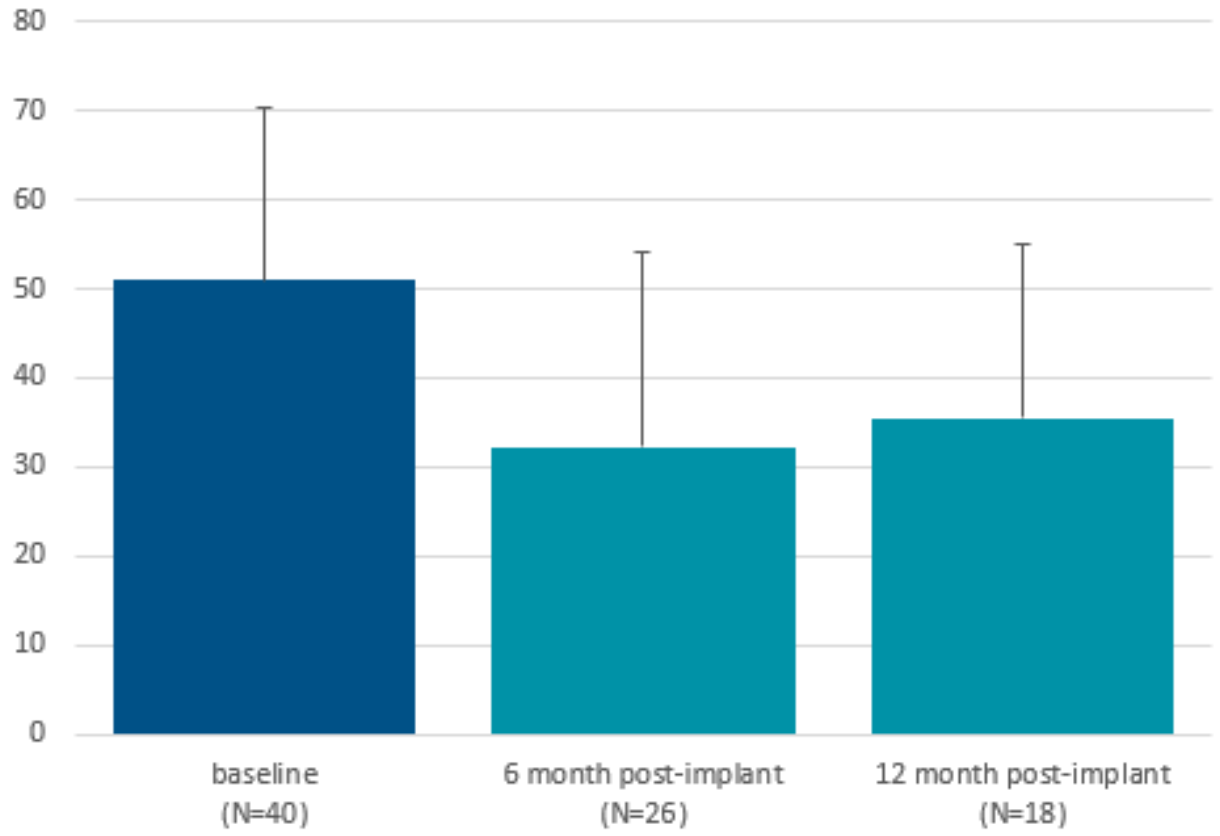
***UTI:** Urinary Tract Infection*

QoL: Maintaining clinically meaningful improvement despite disease progression

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



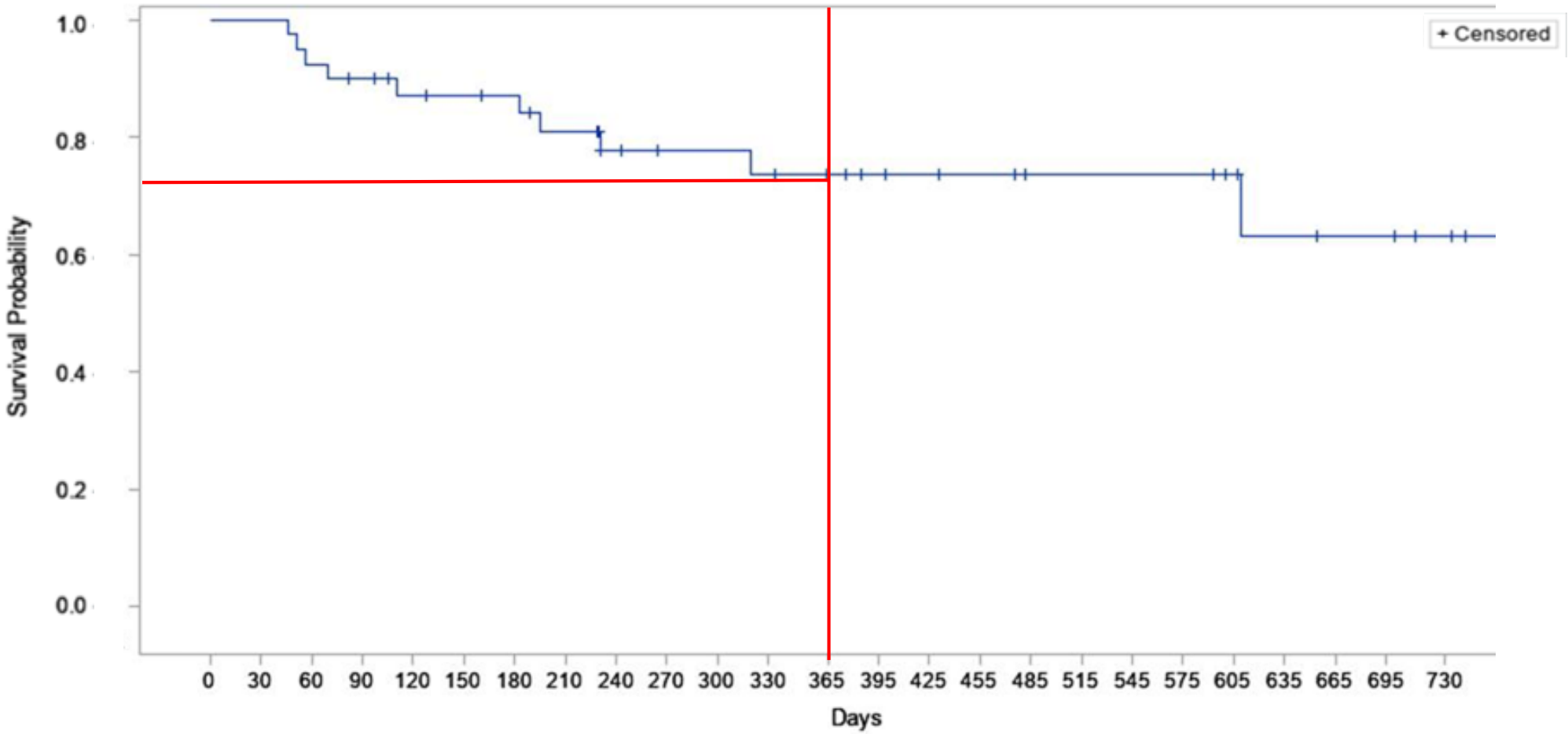
Ascites Q Score (lower is better):



QoL: *Quality of Life*

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

Data supports strong and durable clinical profile of alfapump

✓ Patients with recurrent or refractory ascites have strong preference for a treatment profile like the alfapump vs continuing their standard paracentesis procedures

✓ Patients implanted with the alfapump 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

On track for PMA filing by year end

FDA approval anticipated in H2 2024

Note: Based on data from POSEIDON study, patient preference study and matched interim analysis of NACSELD registry

DSR®

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

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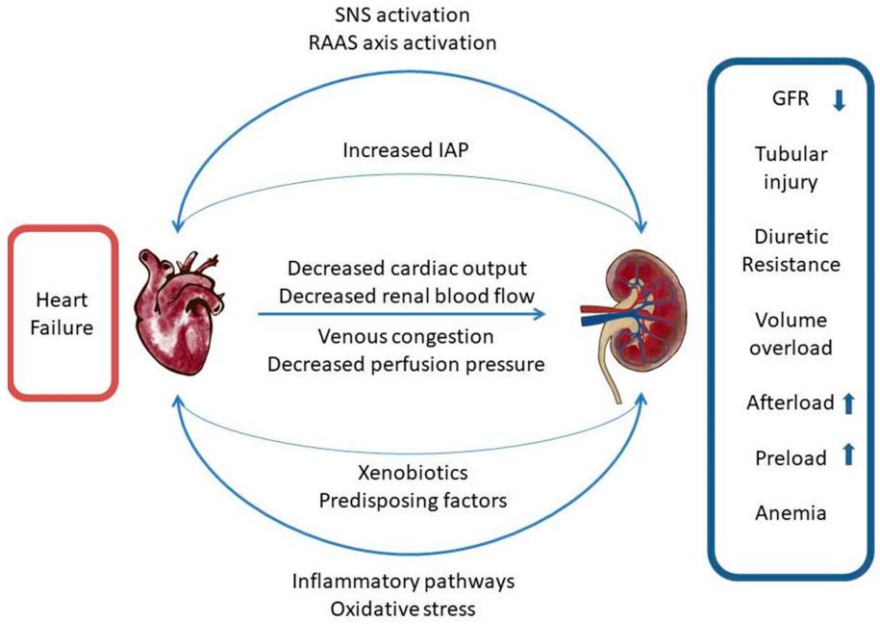
Cardiorenal Syndrome – key clinical challenge in HF

Decongestion is a key component of CRS but the core therapy – loop diuretics – exacerbates the problem

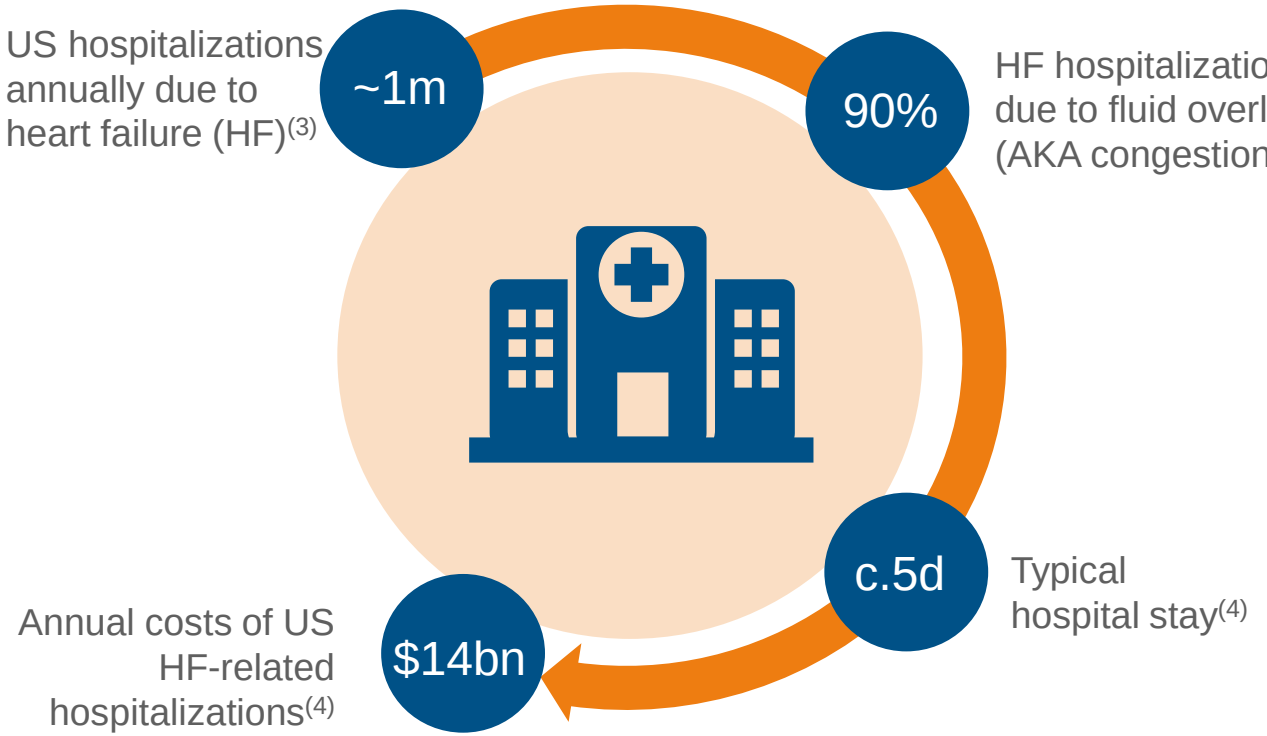
- Combined, and self-reinforcing dysfunction of heart and kidneys with hypothesised complex and interconnected mechanisms
- Clinical profile thought to manifest as self-reinforcing negative feedback cycle that is challenging to break
  - Decreased glomerular filtration, increased renal sodium avidity,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



Clear need for therapies to effectively tackle congestion over a sufficient period of time without the negative consequences of loop diuretics

Congestion is key driver of morbidity & hospitalization

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

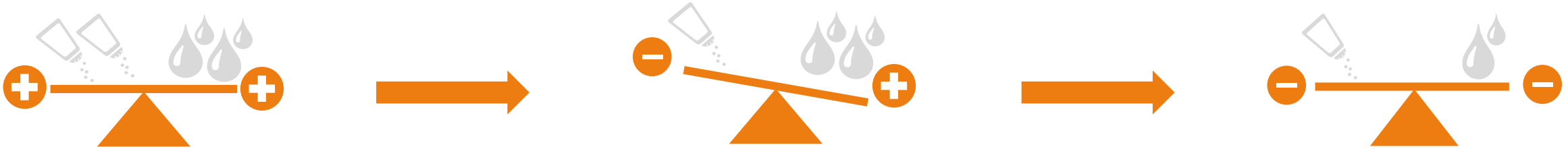


- ***40% of heart failure patients on IV loop diuretics have a poor response(1)***
- ***24% re-admission rate at 30 days(2)***

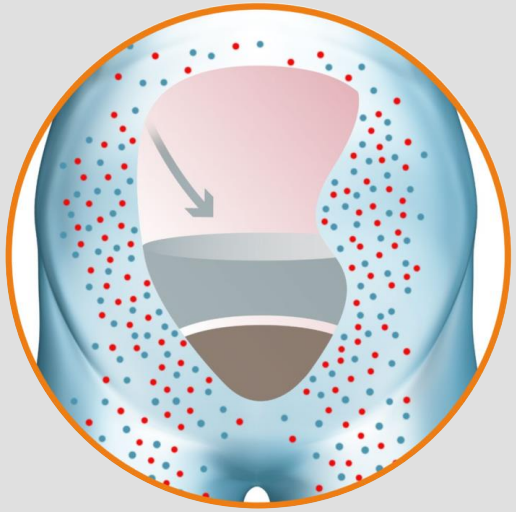
Source 1: Testani, Circ Heart Failure, 2014 & 2016; Source 2: Ross et al. (2010); Source 3: Costanzo et al., J. Am. Coll., 2007; Source 4: Urbich et al. (2020)

DSR (Direct Sodium Removal) – targets the key cause

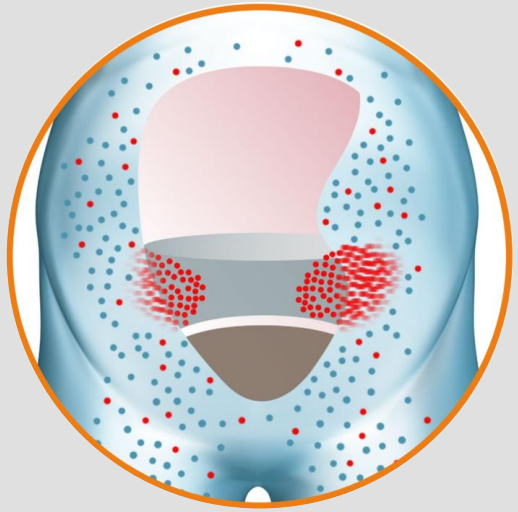
Eliminating fluid spread across the body – working in partnership with the kidneys



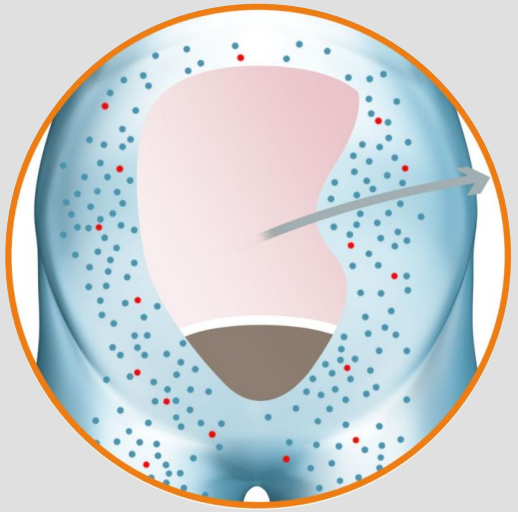
1 Sodium-free DSR product administered to peritoneal cavity



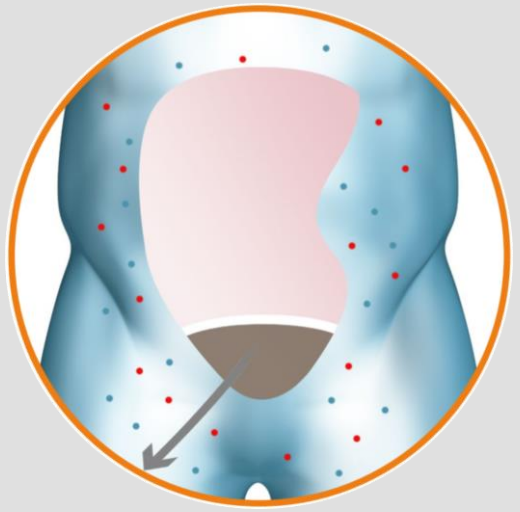
2 Sodium diffuses from body into DSR product



3 DSR product + extracted sodium removed from body



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



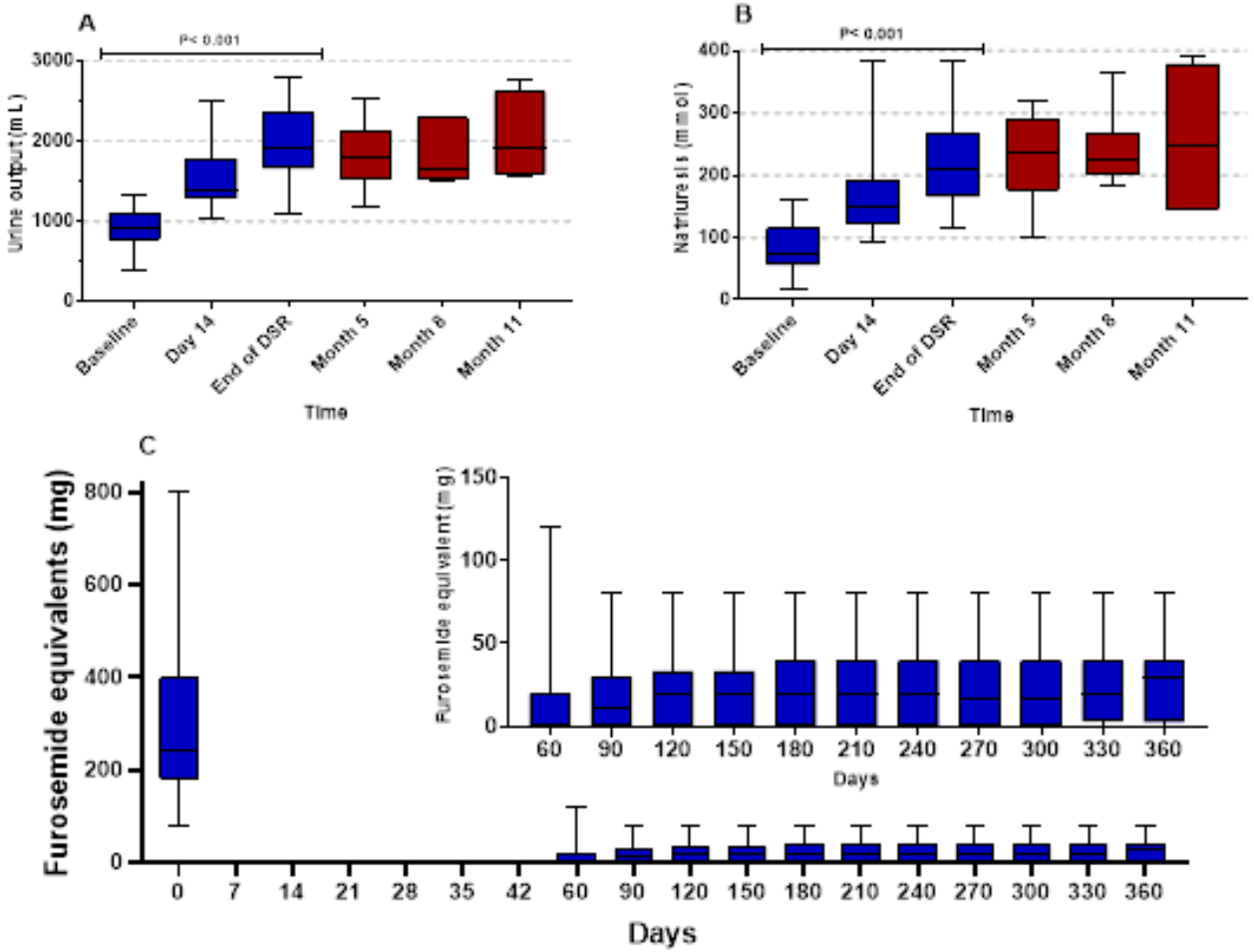
water

sodium

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

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

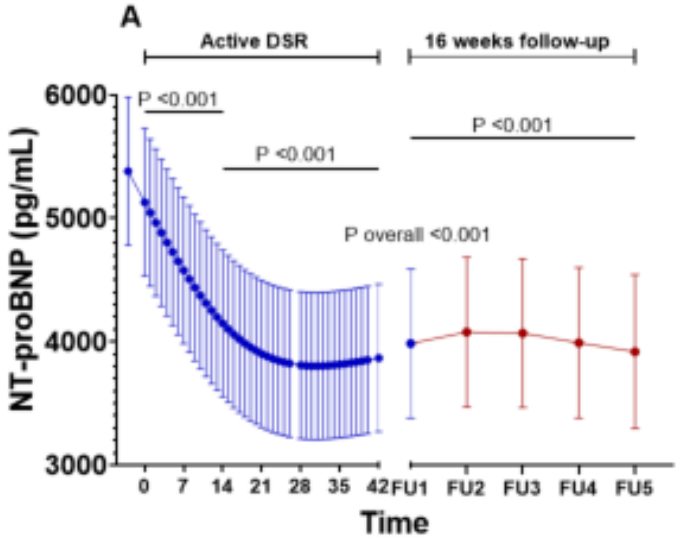
(in furosemide equivs: 1mg oral bumetanide = 20mg oral torsemide = 80mg oral furosemide)

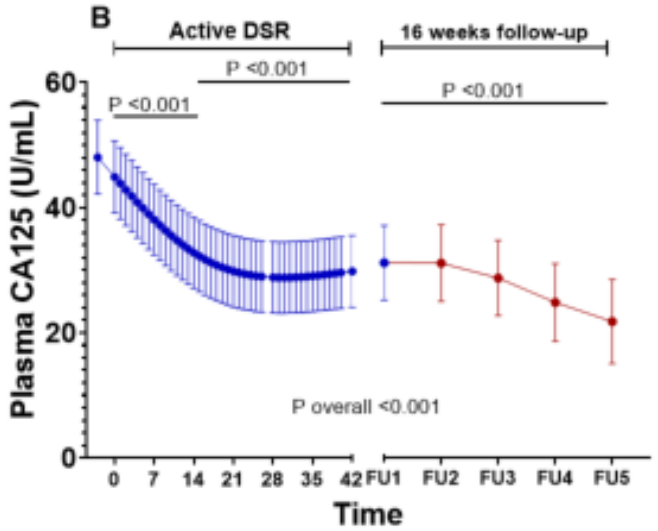
***Blue bars** indicate data from both RED DESERT and SAHARA, and **red bars** indicate data only from SAHARA.*

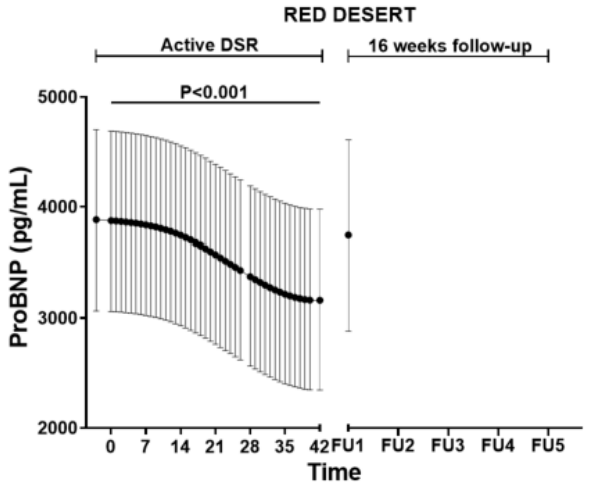
***LD**: Loop Diuretics*

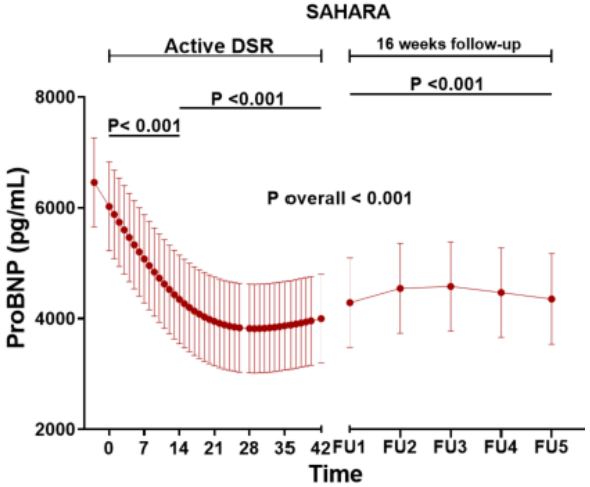
Significant improvement in volume status

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









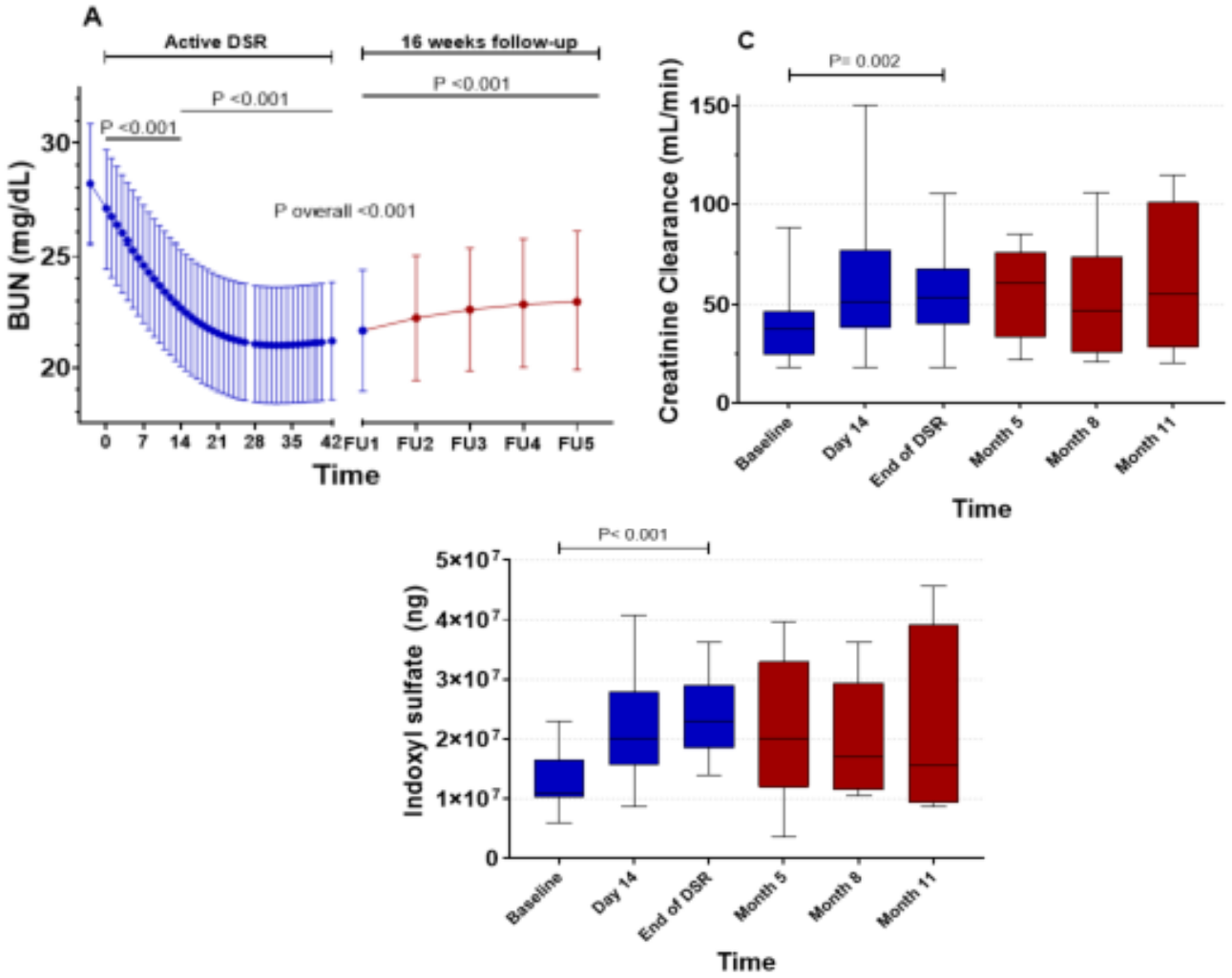
Change in NT-proBNP and Plasma CA125

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



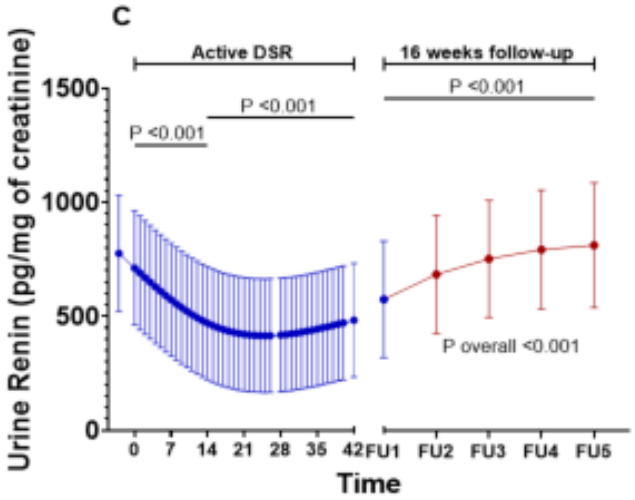
Blood urea nitrogen (BUN) and measured creatinine clearance

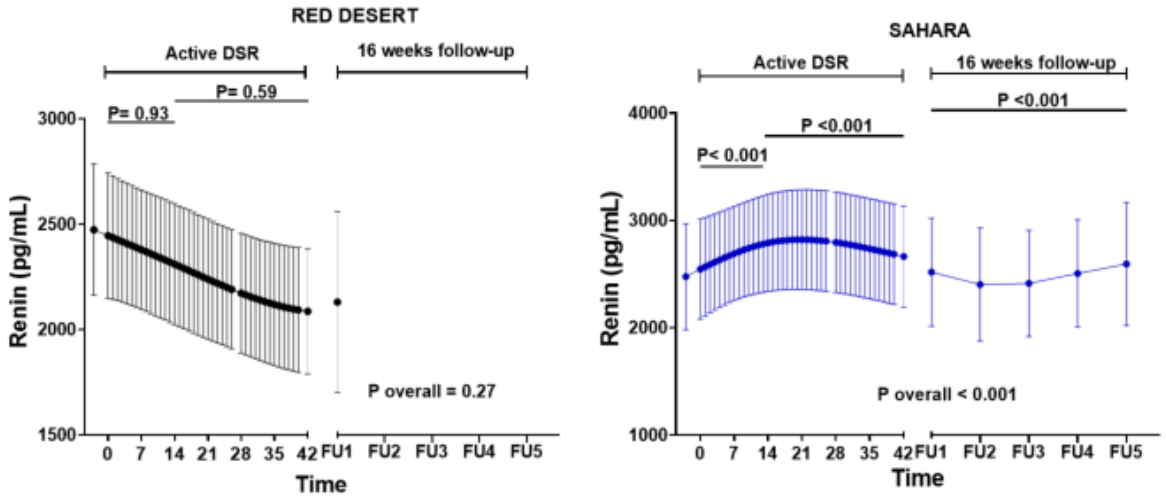
Cumulative 6-hour uremic toxin excretion - indoxyl sulfate

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





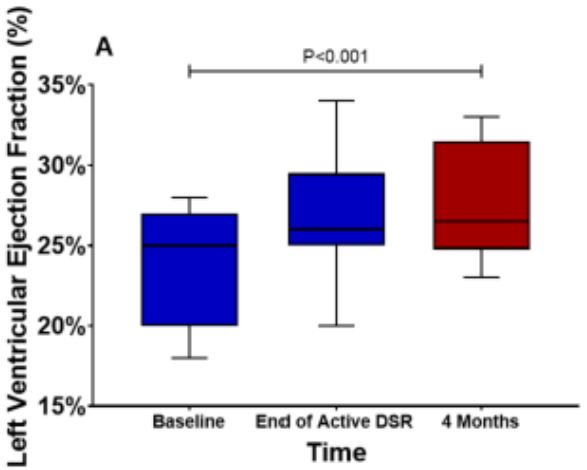
Urine renin – biomarker of local neurohormonal activation at the level of the kidney

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

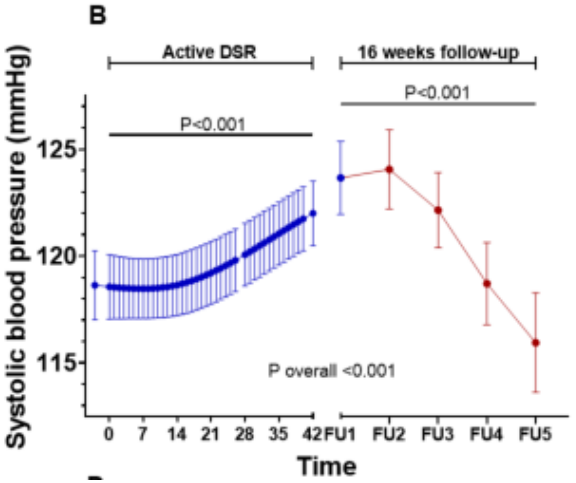
Data are presented as *Mean (SEM)* over time – active volume removal in SAHARA patients driving increase in renin

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.*

DSR – breaking the CRS vicious cycle

Detailed biomarker analysis aligns with improved clinical outcomes in RED DESERT and SAHARA

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 and natriuretic peptide signaling
- ✓ No significant increase in renin or aldosterone (after adjustment for weight loss during decongestion)

Leading to improved clinical outcomes

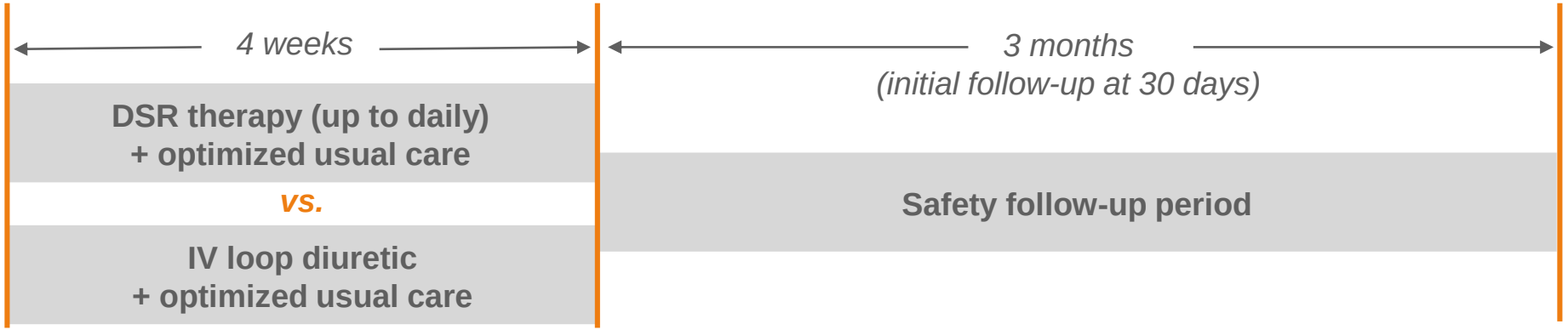
- ✓ No congestion-related heart failure re-hospitalizations
- ✓ One class improvement of NYHA status
- ✓ Over 75% reduction in predicted one-year mortality*

** 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

First two US patients successfully treated with DSR 2.0

MOJAVE non-randomized cohort

- At baseline:
  - Heart failure patients with preserved ejection fraction (HFpEF) and severe diuretic resistance
  - High dose loop diuretics – furosemide equivalent dose of 1,200 and 800 mg per day

- After DSR treatment period:
  - No need for any loop diuretics
  - Near normalization of diuretic response, with dramatic increase in 6-hour urinary sodium excretion
  - Broad improvement in kidney function and stable cardiovascular status maintained
  - No clinically relevant changes in serum sodium levels or progressive hyponatremia and no serious adverse events

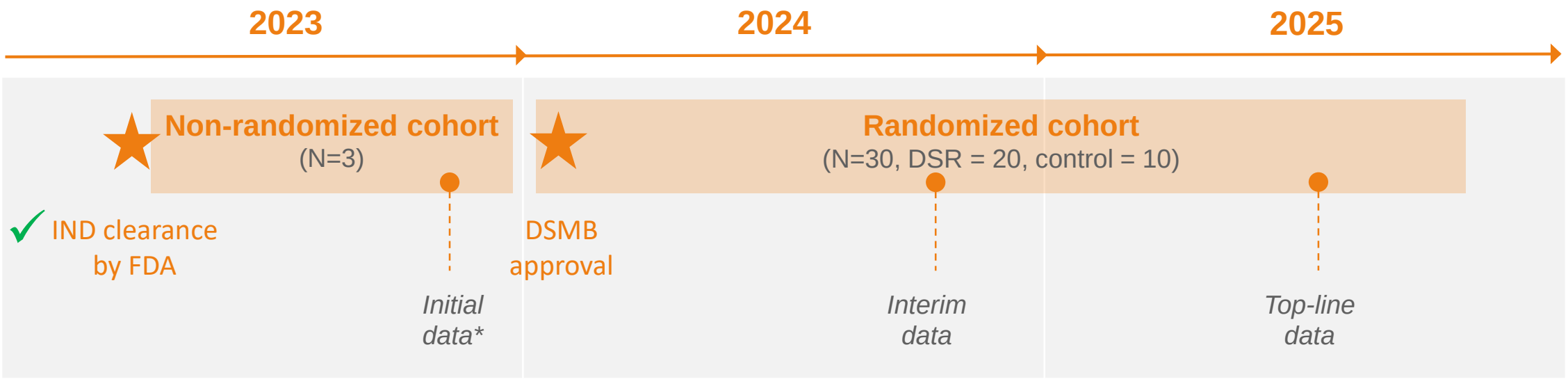
Difference 4-week post-treatment vs baseline	Patient 1	Patient 2
Increase in 6-hour mmol sodium excretion	+195%	+712%
Decrease in blood urea nitrogen	-65%	-52%
Increase in eGFR	+64%	+49%

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

On track to start randomized cohort in Q1 2024

Top-line data from all three patients in non-randomized cohort planned by year-end

- All three non-randomized cohort patients have been enrolled
  - Patient 1: 9.5 weeks post DSR treatment commencement without loop diuretics
  - Patient 2: 4 weeks post DSR treatment commencement without loop diuretics
  - Patient 3: enrolled, with completion of DSR treatment and initial follow-up planned before year end



Top-line data in mid 2025 intended to deliver the clinical data package for partnering

** Data from three patients in non-randomized cohort*

Fluid overload – large markets with strong growth

Poor clinical outcomes and high treatment costs when diuretics are no longer beneficial

alfapump in liver disease

- Market growing to over $2.5 billion by 2035(1)
- FDA breakthrough device / Approved in EU
- Successful North American POSEIDON pivotal study – primary endpoints met, strong clinical profile
- PMA filing planned for Q4 ’23 with FDA approval anticipated in H2 ‘24
- Direct sales in US
- Strong reimbursement profile – existing DRGs, NTAP and TCET opportunity

DSR in heart failure

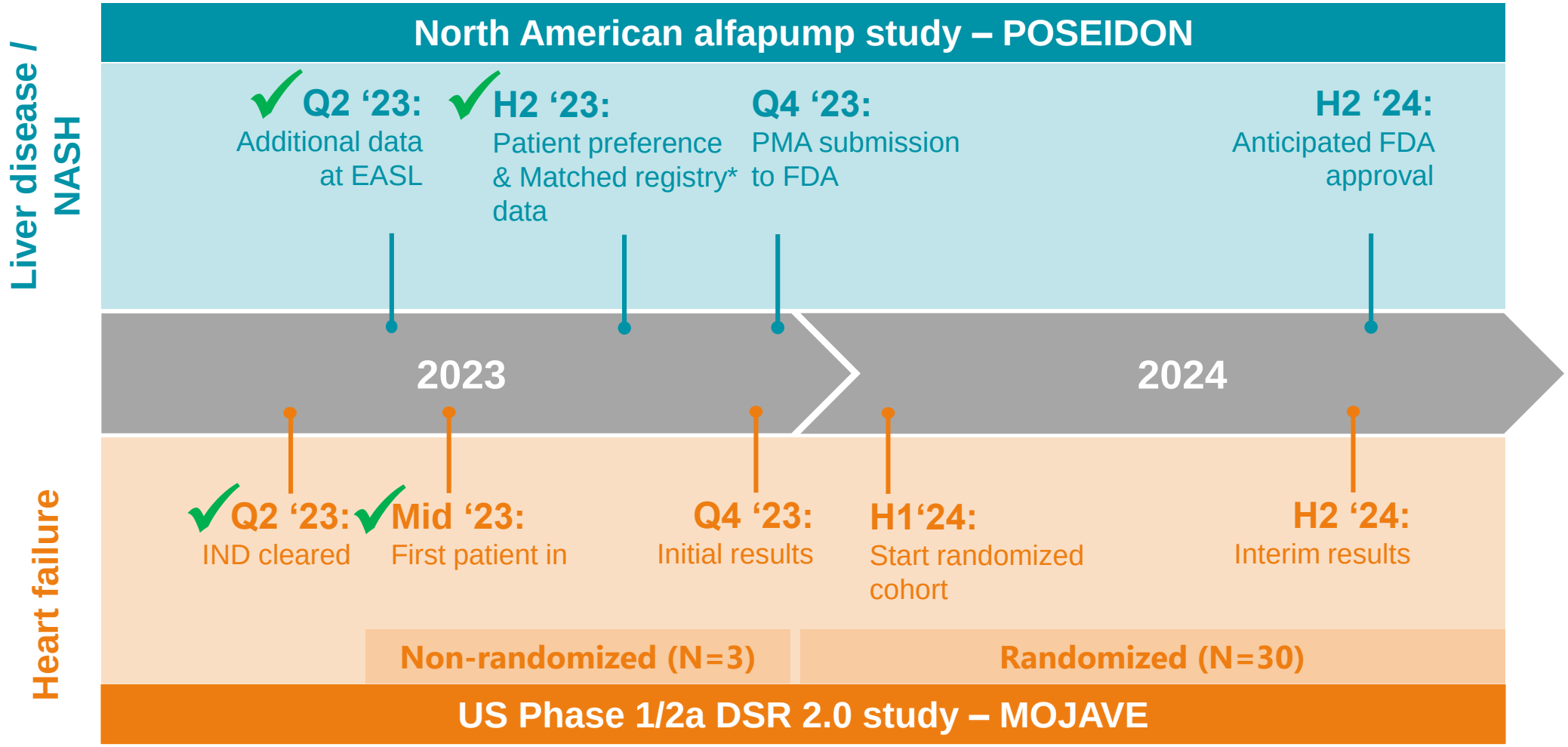
- Multi-billion market opportunity
- Novel treatment for cardiorenal syndrome (CRS)
- Clinical proof-of-concept as disease-modifying drug therapy
- Transitioning to DSR 2.0; low development risk, improved profile & strong IP
- US Ph. 1/2a randomized controlled study (MOJAVE) started; data from first three patients in Q4 ‘23
- Partnering based on MOJAVE readout planned for ‘25

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

*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*

***PMA:** Pre-Market Approval; **DRG:** Diagnosis Related Group (hospital payment code); **NTAP:** New Technology Add-on Payment; **TCET:** Transitional Coverage of Emerging Technologies*

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*

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