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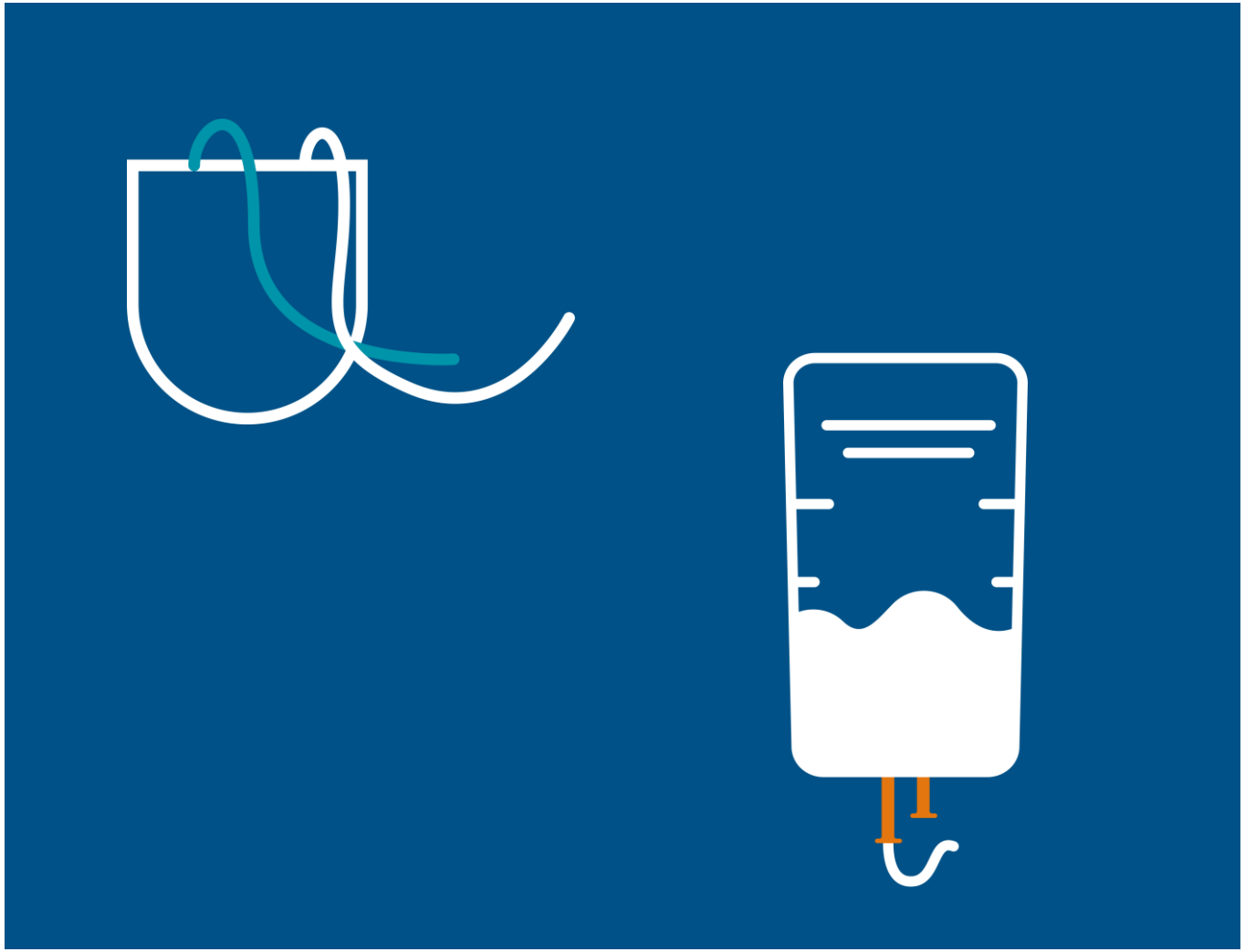

Pioneers in the treatment of fluid overload

Transforming lives in
liver disease, heart failure & cancer

Investor presentation – July 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.

Fluid overload – large markets with strong growth

Diuretic-resistance is common and current treatment options are extremely limited

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

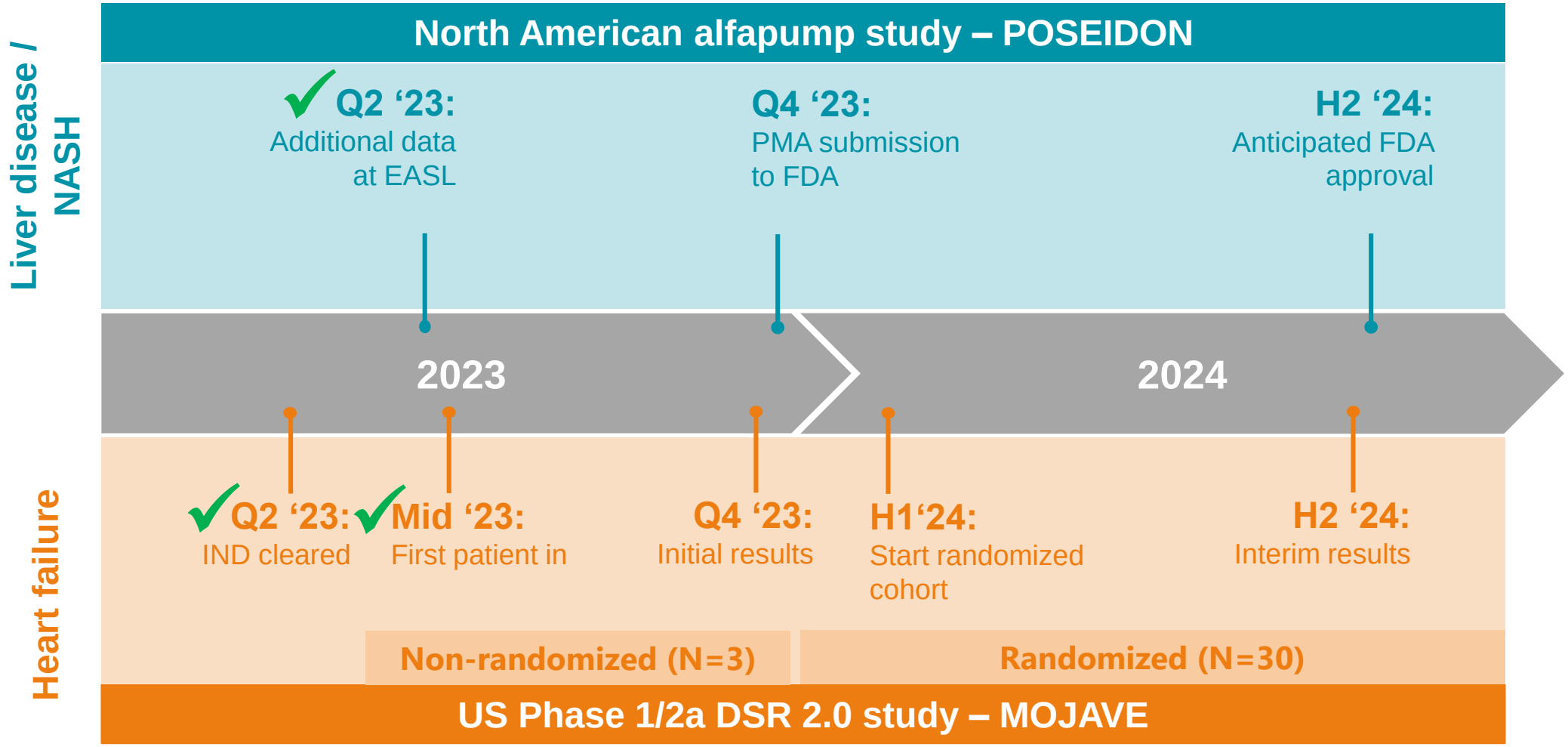
- Multi-billion market opportunity
- Clinical proof-of-concept as disease-modifying heart failure drug therapy
- Transitioning to DSR 2.0; low development risk, improved profile & strong IP
- US Ph. 1/2a randomized controlled study (MOJAVE) started; initial data planned for Q4 ‘23
- Partnering based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

Growth in liver cirrhosis due to NASH and breakthrough DSR innovation 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



alfapump®

Proven step change in the treatment of liver refractory ascites

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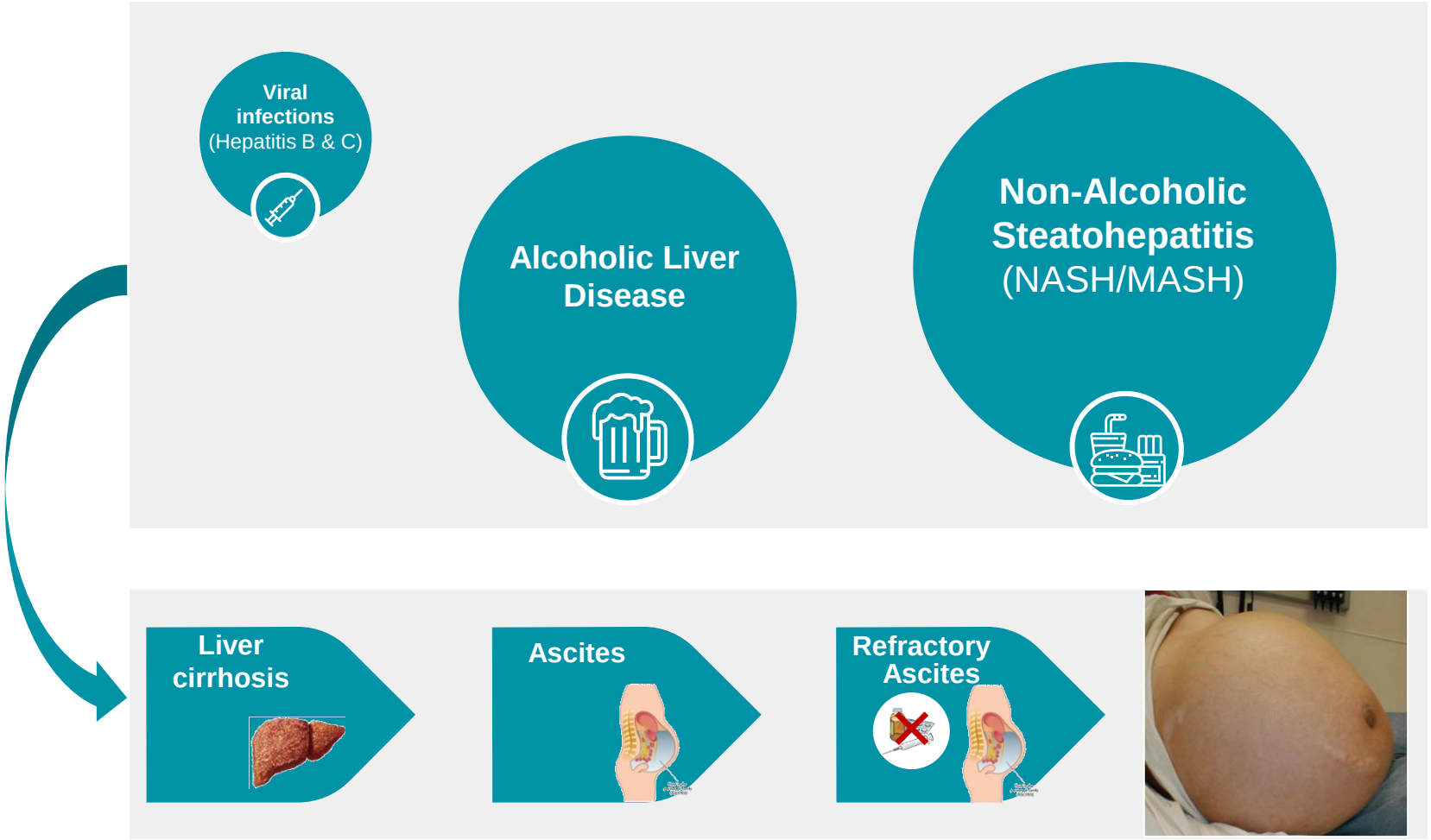
Refractory ascites – key complication of liver cirrhosis

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



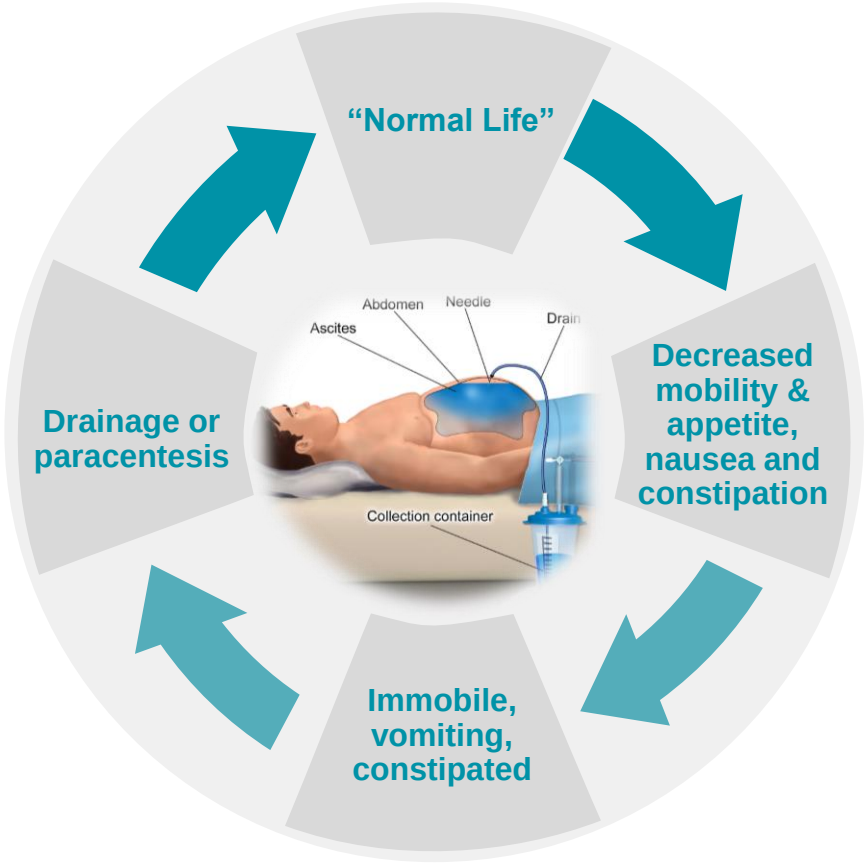
***NASH**: non-alcoholic steatohepatitis, also referred to as MASH (metabolic dysfunction-associated steatohepatitis) as per new fatty liver disease nomenclature (Hepatology, June 2023)*

Clear limitations of existing treatment options

Little innovation or new development – transplant is a partner not competitor

Paracentesis (LVP / drainage)

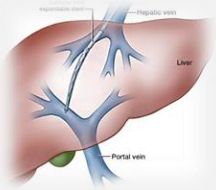
Painful, burdensome, short term benefit, QoL impact



Permanent Catheter System

External Catheter, Risk for Infections / Blockage

TIPS



Complications, Contraindications

Liver transplantation

High Cost,
Limited Availability
Long Waitlist

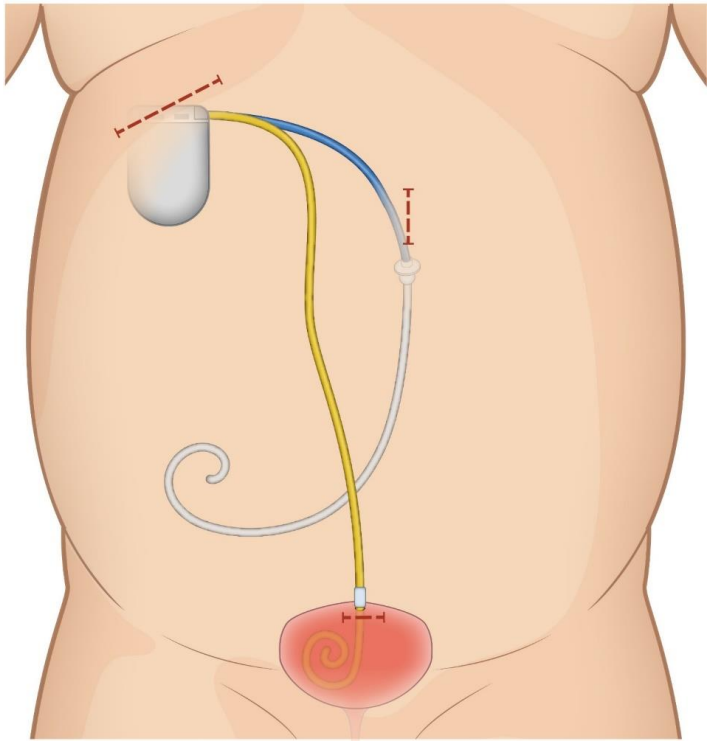
Source: Presentation of Dr. Rajiv Jalan at EASL in 2018, Large Volume Paracentesis (LVP) treatment cycle for refractory ascites

TIPS: *Transjugular Intrahepatic Portosystemic Shunt*

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



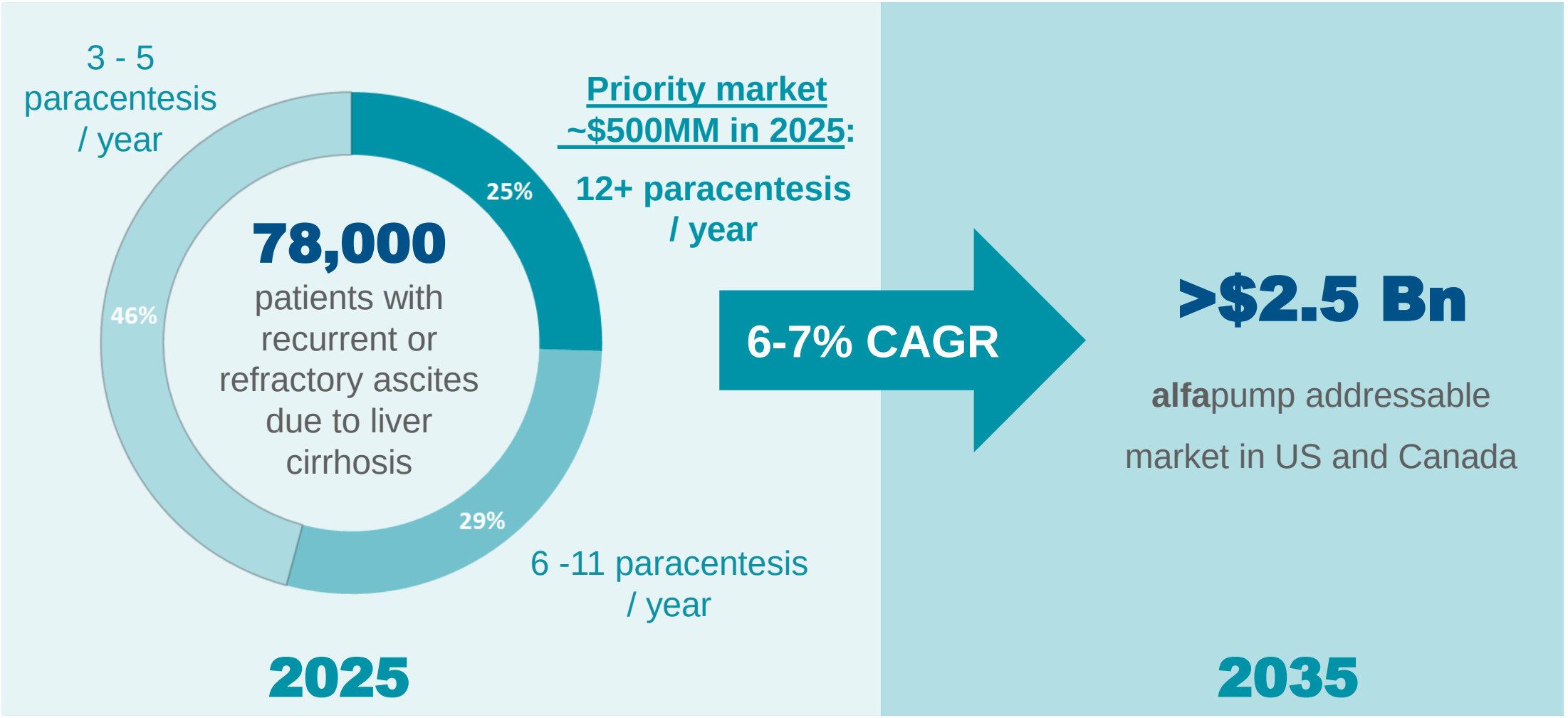
Breakthrough Device Designation

Over 1,000 systems implanted

Strong IP barriers through extensive patent portfolio & know-how

Large and strongly growing North American market

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

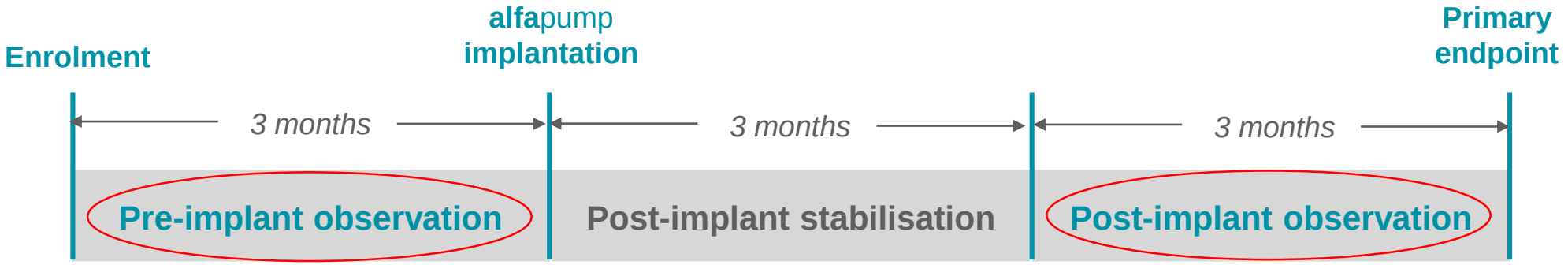


*Sources: Based on US and Canada market assessment by international consulting group, using claims analysis for commercial and CMS (Center for Medicare and Medicaid Services) patients requiring paracentesis procedure with liver disease diagnosis codes; Medicare Inpatient & Outpatient Hospital Standard 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 (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

PMA filing planned for Q4 2023 / FDA approval anticipated in H2 2024

** Post vs Pre-implant observation period*

Note: Secondary endpoints on long-term follow-up of patients, up to 24 months post-implant

POSEIDON – strong clinical profile of alfapump

Primary and key secondary endpoints presented by Prof. Wong, PI, at leading international liver congress

- ✓ **Effective in control of ascites, "virtually eliminating needle paracentesis"**
- ✓ **NASH is already a key driver of decompensated cirrhosis**
- ✓ **Safety in line with expectations**
  - Six pumps were explanted: three due to skin erosion & three due to moderate bladder discomfort
  - Despite disease progression:
    - Similar number of Major Adverse Events (MAEs) in pre- and post-implant period
    - Comparable number of serious infections in pre- and post-implant period
    - Stable kidney function over long-term follow-up
- ✓ **Clinically meaningful and statistically significant improvement in quality of life***
- ✓ **One-year survival probability of 70%, comparing favorably to literature citing 50%**(1)

** At six months post-implantation compared to baseline*

Source 1: Biggins et al., Hepatology, Vol. 74, No. 2, 2021, AASLD Practice Guidance; Moreau R et al., Liver International 2004: 24: 457-464; Note: POSEIDON study not powered for survival

Attractive pricing with derisked reimbursement

Existing DRG payment and breakthrough device designation de-risk reimbursement of alfapump

Coding – Strong existing position with potential for further upside

- Existing hospital DRG payment for **alfa**pump procedure supports **alfa**pump price of **at least $25K** (gross margin of over 75%)
- US DRG payments of $60-70K in target hospitals*
- 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

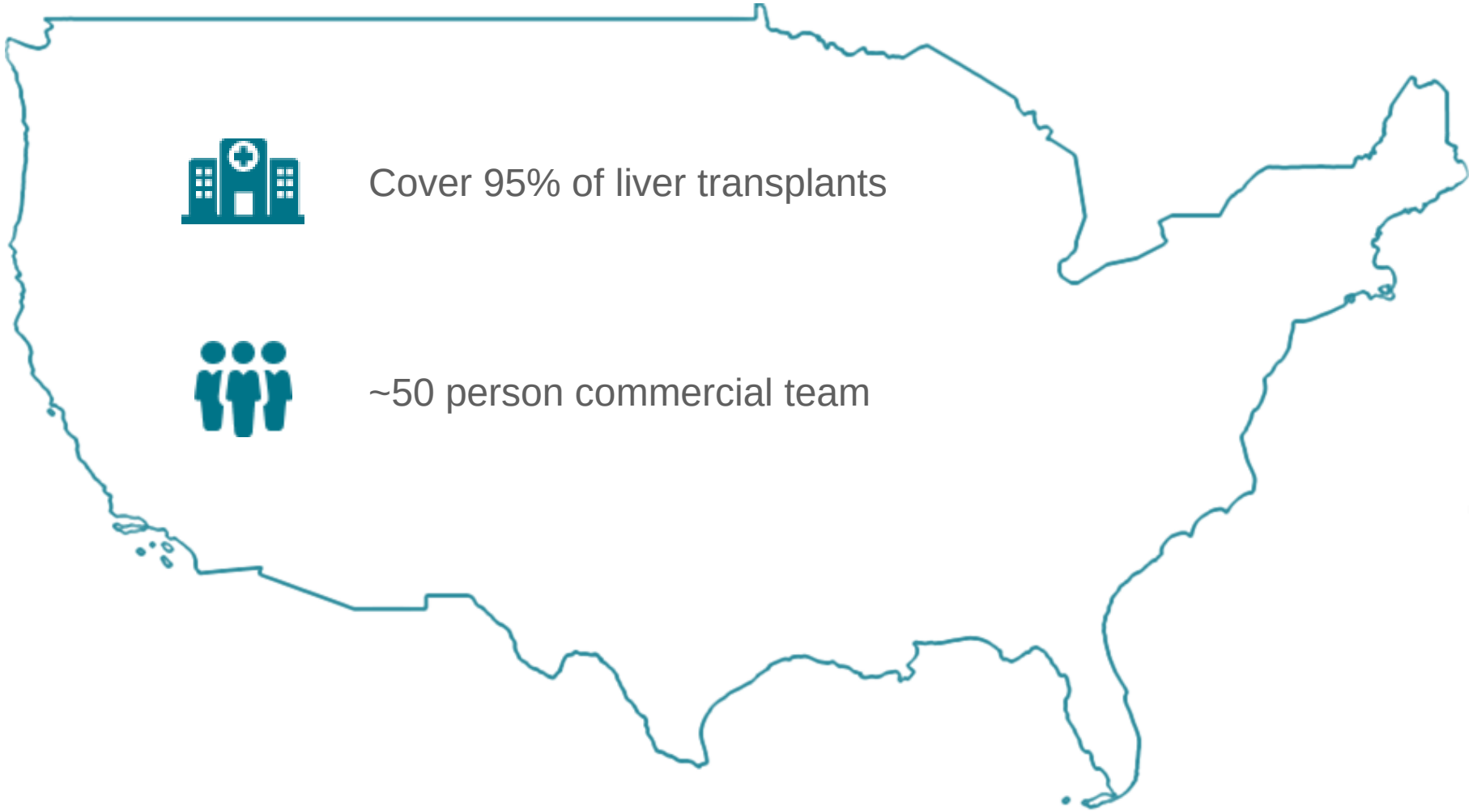
Medicare will be dominant payer
Additional potential from Veterans Affairs

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

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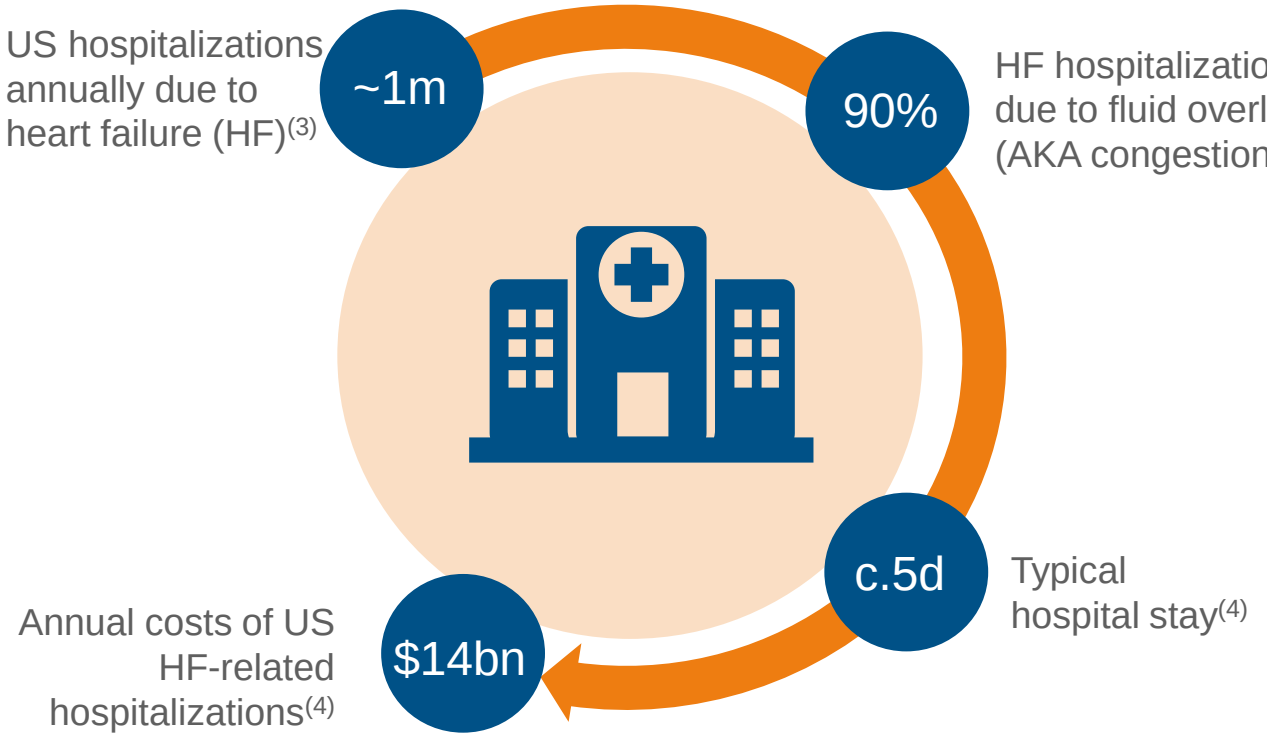
Congestion is key driver of morbidity & hospitalization

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

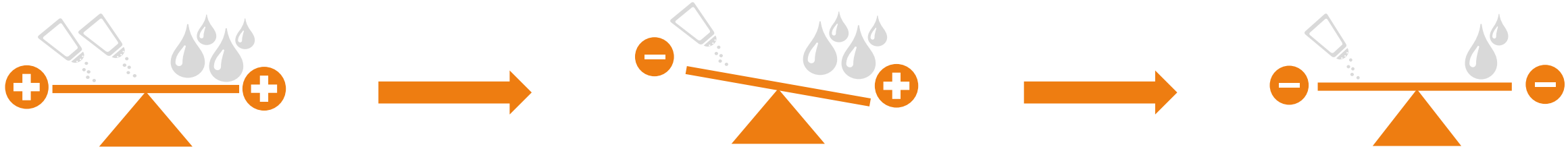


- *40% of heart failure patients on IV loop diuretics have a poor response(1)*
- *24% re-admission rate at 30 days(2)*

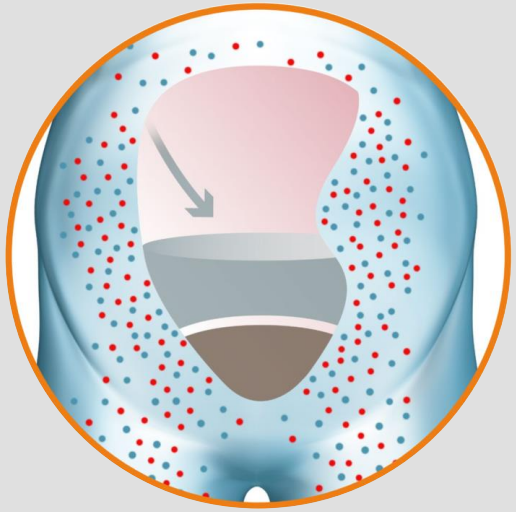
Source 1: Testani, Circ Heart Failure, 2014 & 2016; Source 2: Ross et al. (2010); Source 3: Costanzo et al., J. Am. Coll., 2007; Source 4: Urbich et al. (2020)

DSR (Direct Sodium Removal) – targets the key cause

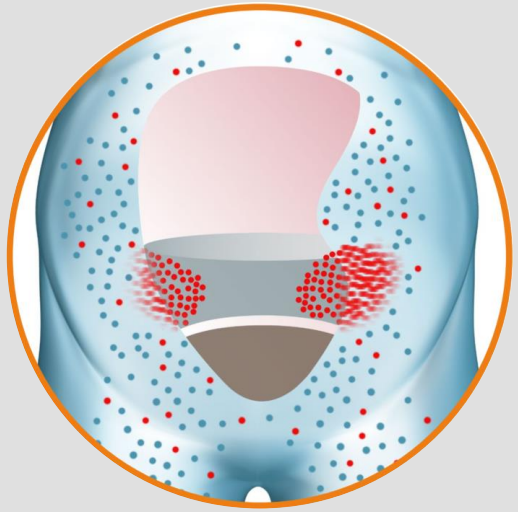
Eliminating fluid spread across the body – working in partnership with the kidneys



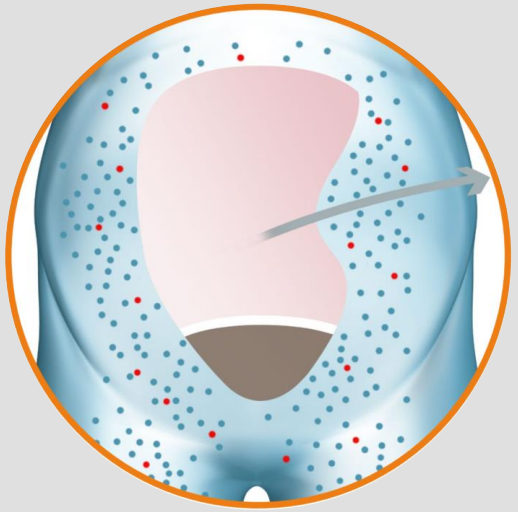
1 Sodium-free DSR product administered to peritoneal cavity



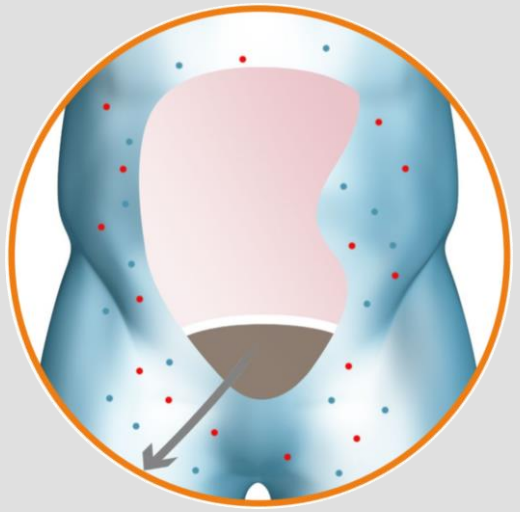
2 Sodium diffuses from body into DSR product



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

Disease-modifying heart failure drug therapy

RED DESERT and SAHARA deliver clinical proof-of-concept with long-lasting clinical benefits

Effective decongestion and durable improvements in cardio-renal health

- ✓ Safe, effective and rapid elimination of fluid overload / restoring euvolemia
- ✓ Considerable benefit in eGFR and NT-proBNP
- ✓ Dramatic and sustained improvement in diuretic response

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*

"These 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

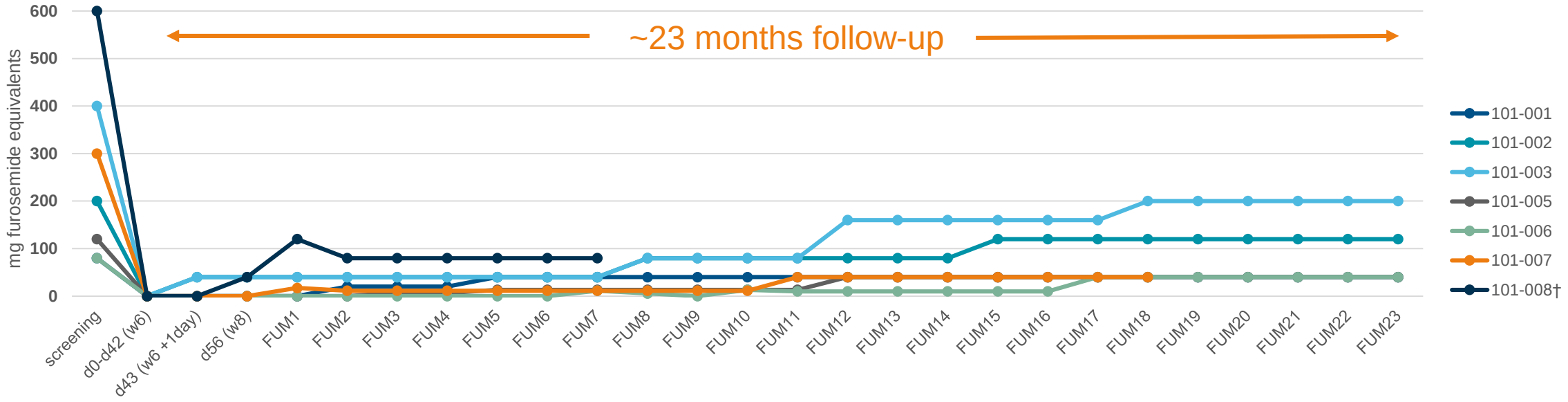
** Based on Seattle Heart Failure Model*

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

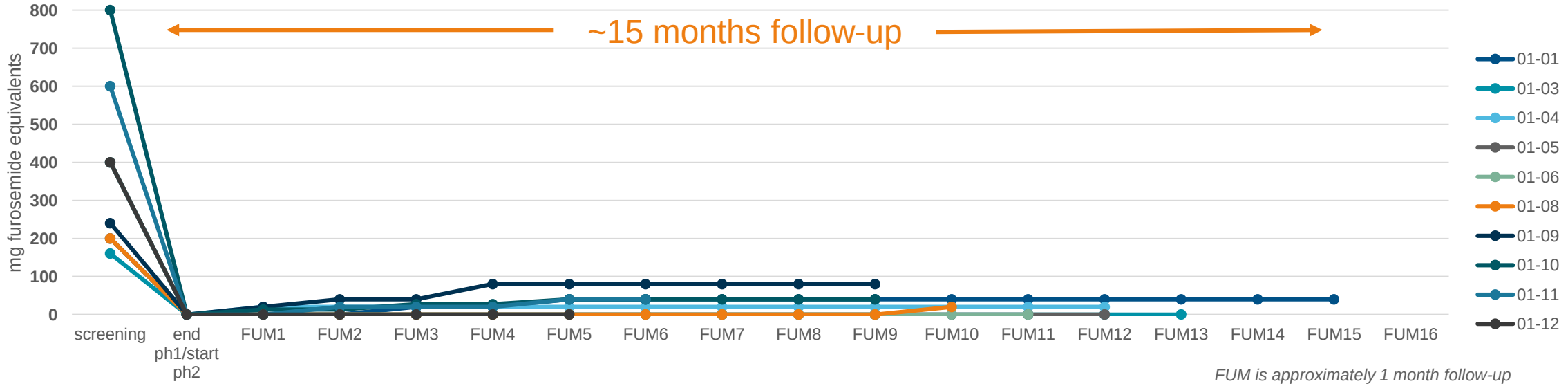
Long-term improvement in cardio-renal status

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

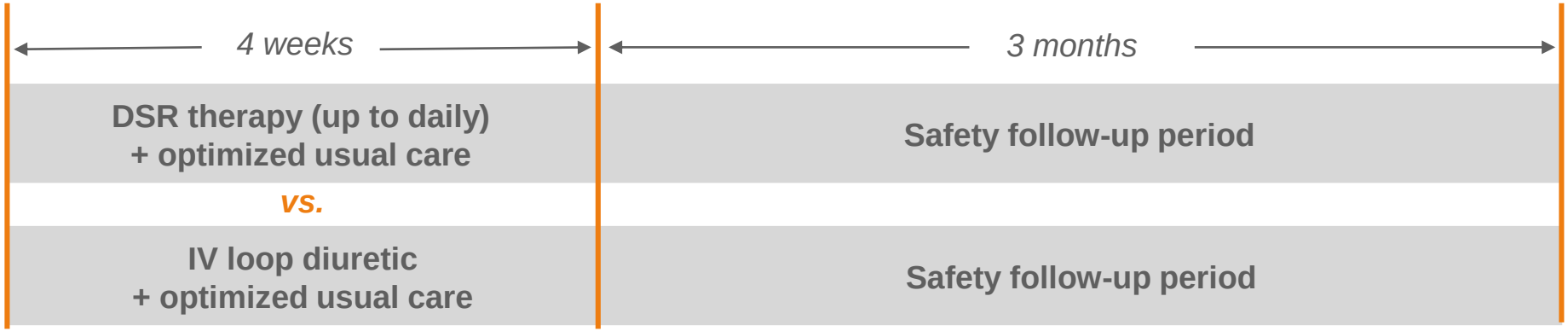
DSR 2.0 improves therapeutic and safety profile

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

MOJAVE – Phase 1/2a randomized controlled US study

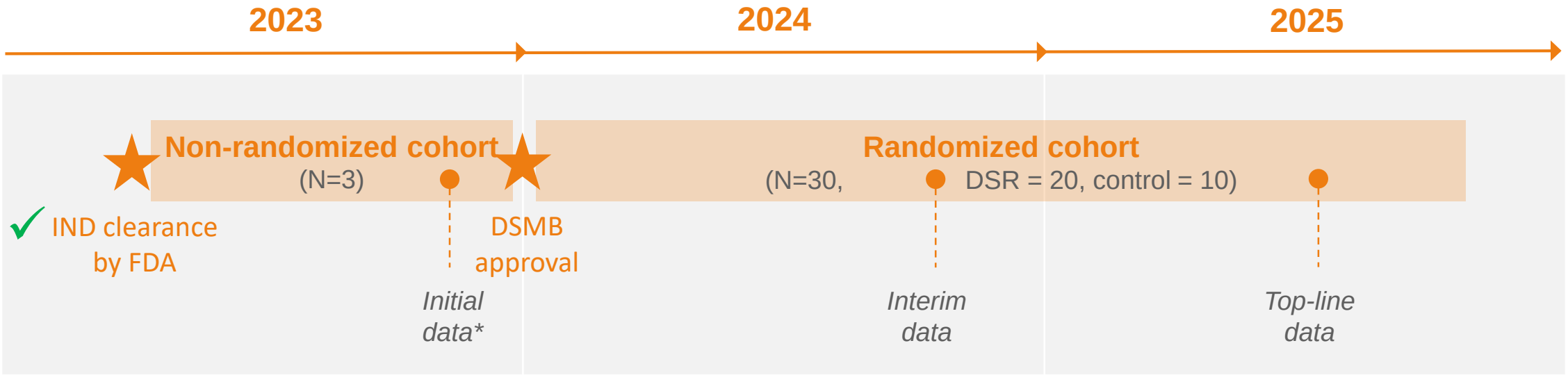
Seeking to replicate SAHARA outcomes in US study of heart failure patients with persistent congestion



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

MOJAVE – initial data expected in Q4 2023

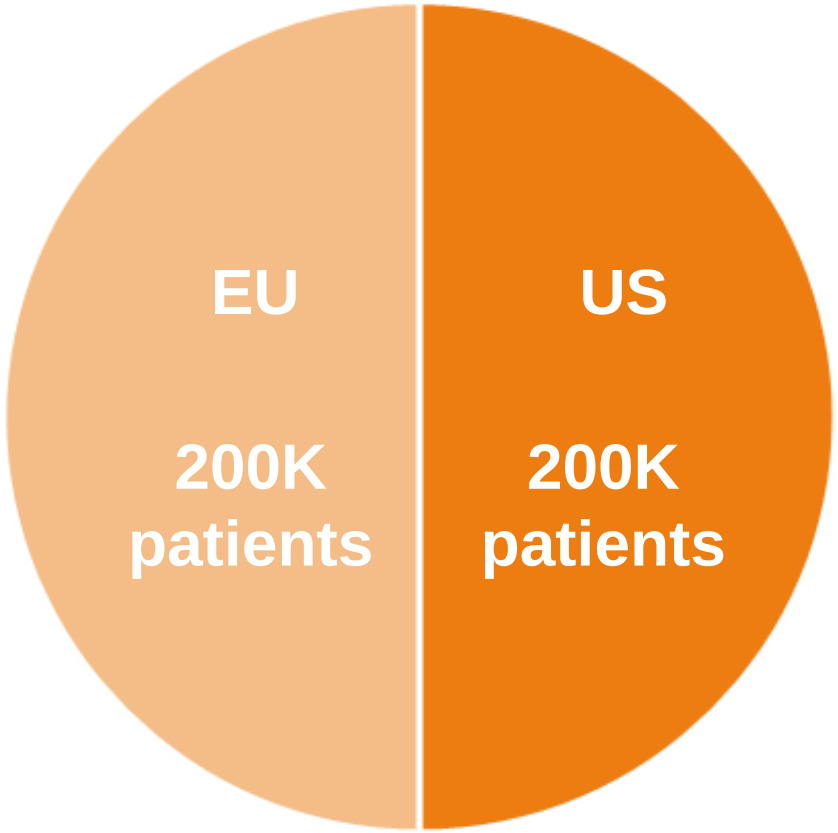


Top-line data in mid 2025 intended to deliver the clinical data package for partnering

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

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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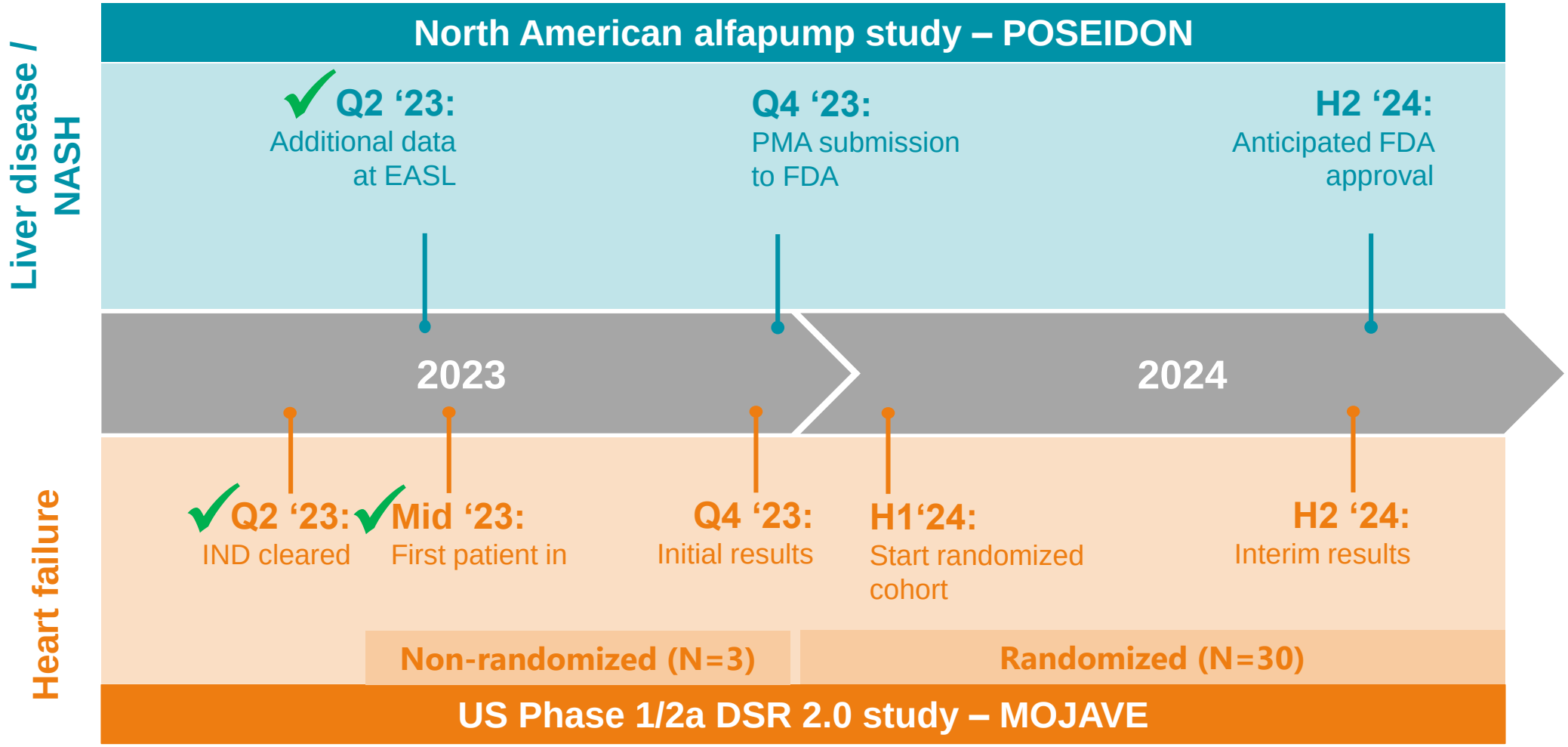
Strong outlook for key value drivers



Leader in large and growing markets with unmet needs

alfapump® in liver disease – market potential growing to over $2.5 billion by 2035(1)

- NASH is changing liver cirrhosis market and driving strong growth
- Approved in EU / FDA breakthrough device status / Strong IP portfolio
- North American pivotal study – reported strong primary and key secondary endpoint data
- FDA approval expected in 2024 / Go direct to liver transplant centers / derisked reimbursement

DSR® in heart failure – multi-billion market opportunity in EU and US

- Clinical proof-of-concept as disease-modifying heart failure drug with DSR 1.0
- Transitioning to proprietary DSR 2.0 – low development risk, improved profile & strong IP
- MOJAVE US randomized controlled Ph. 1/2a started – initial data planned for Q4' 23
- Partner based on MOJAVE top-line data in '25

*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*

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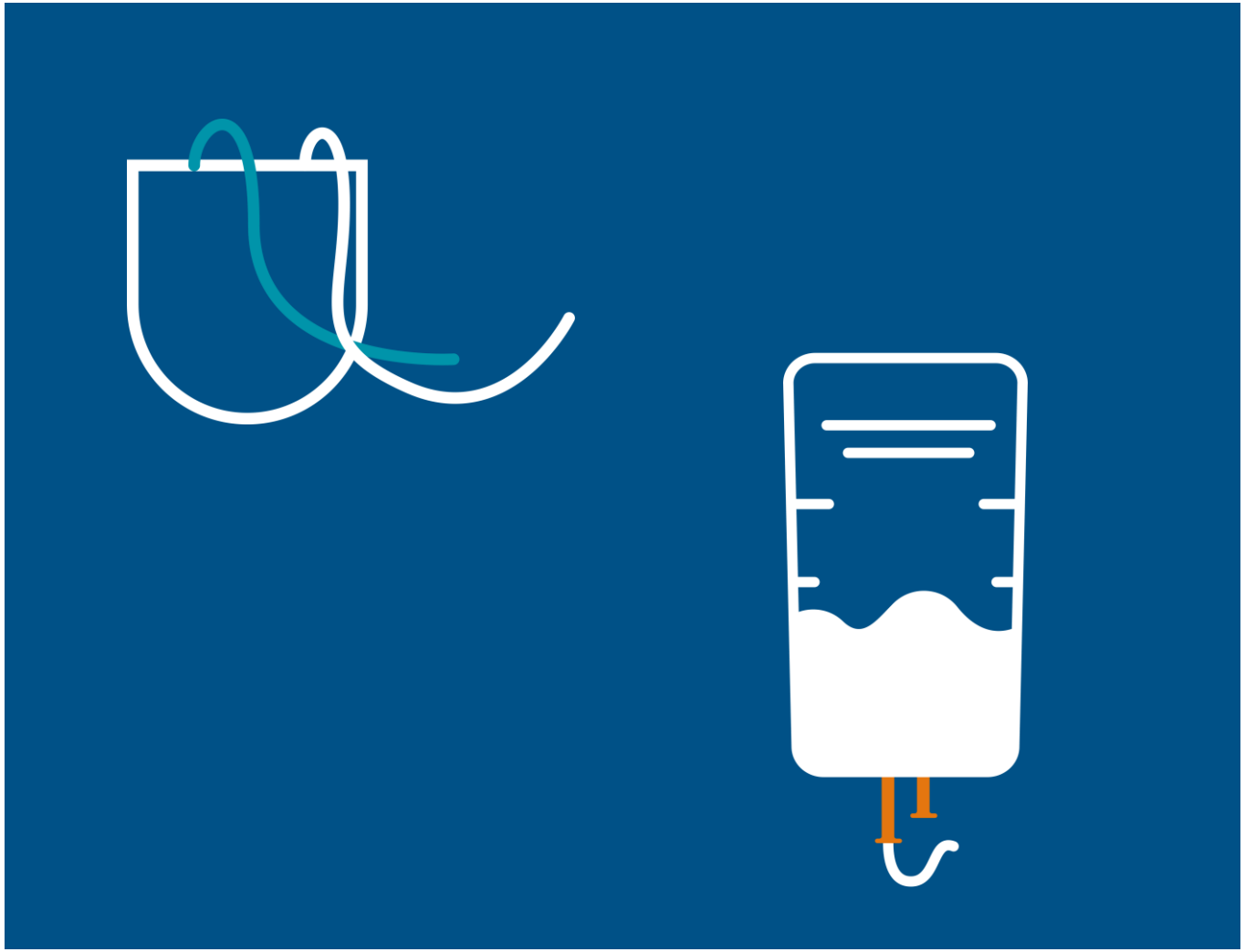

Back-up

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:

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Board Chairman

Rudy Dekeyser
Director

Wim Ottevaere
Director

Jackie Fielding
Director

Doug Kohrs
Director

Alex Clyde
Director

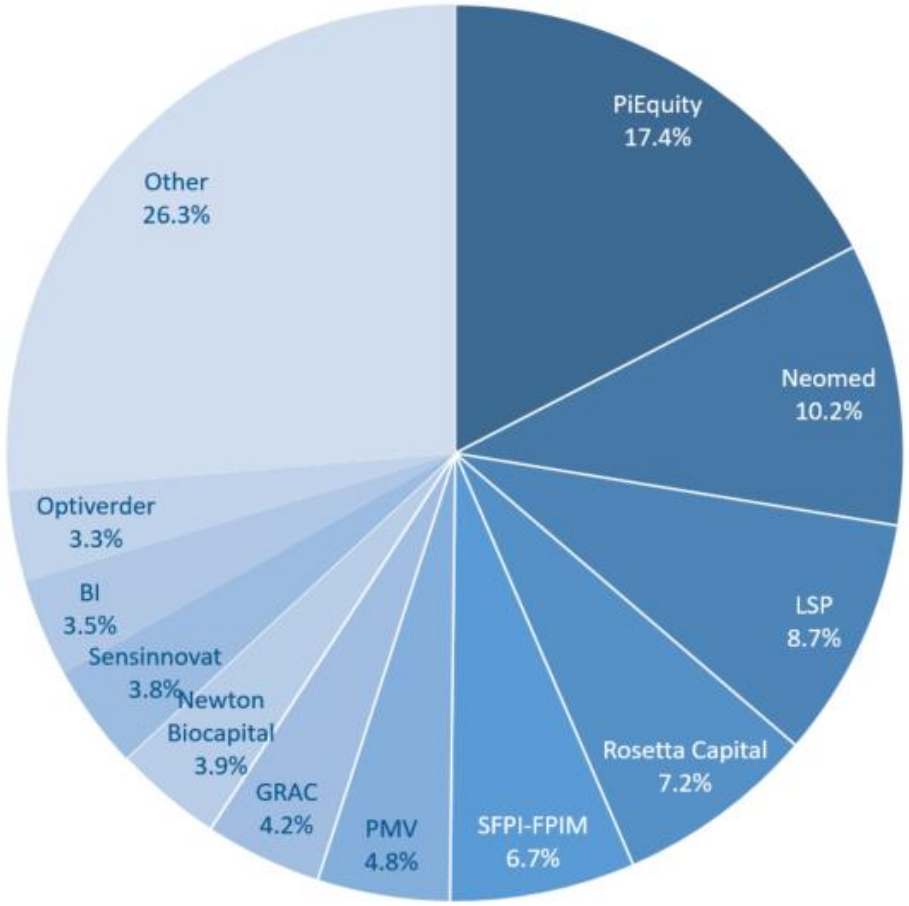
Kenneth Macleod
Director

Ian Crosbie
Chief Executive Officer

Shareholders base and financial overview

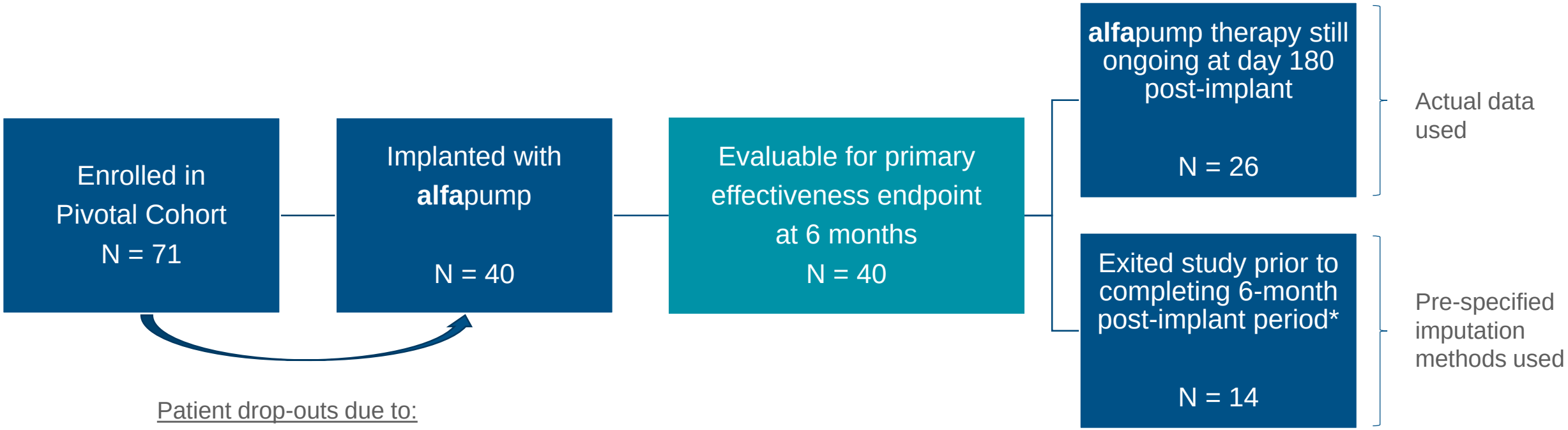
Ticker: SEQUA – Euronext Brussels

- 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 – Jeroen Van den Bossche
  - Van Lanschot Kempen – Suzanne van Voorthuizen
- Cash (31 December 2022): €18.9M
- 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

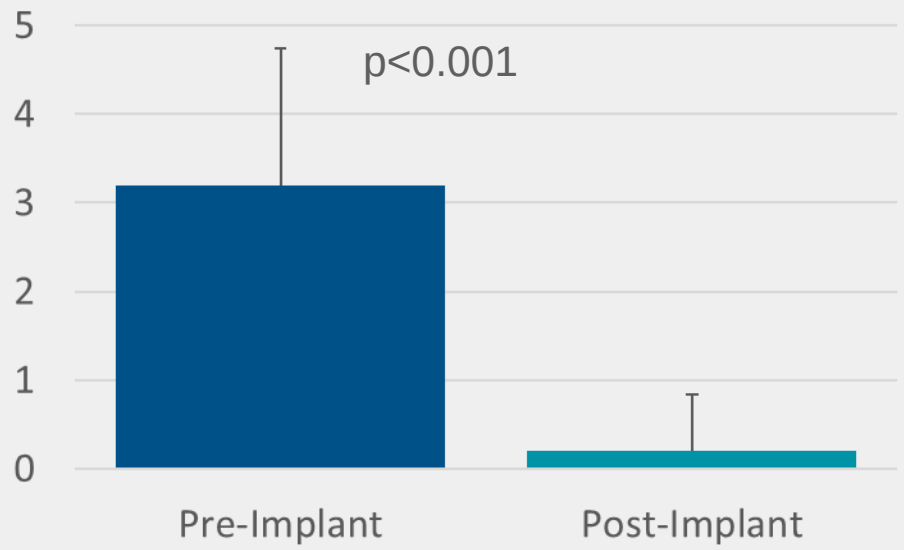
* *Some patients may have more than one etiology of cirrhosis*

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

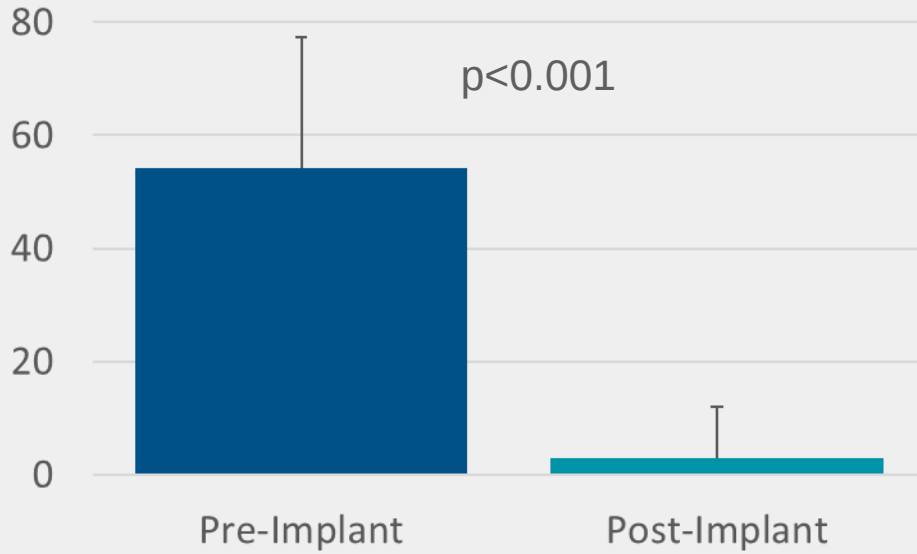
POSEIDON: Primary effectiveness endpoints exceed predefined thresholds for study success*

- **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:



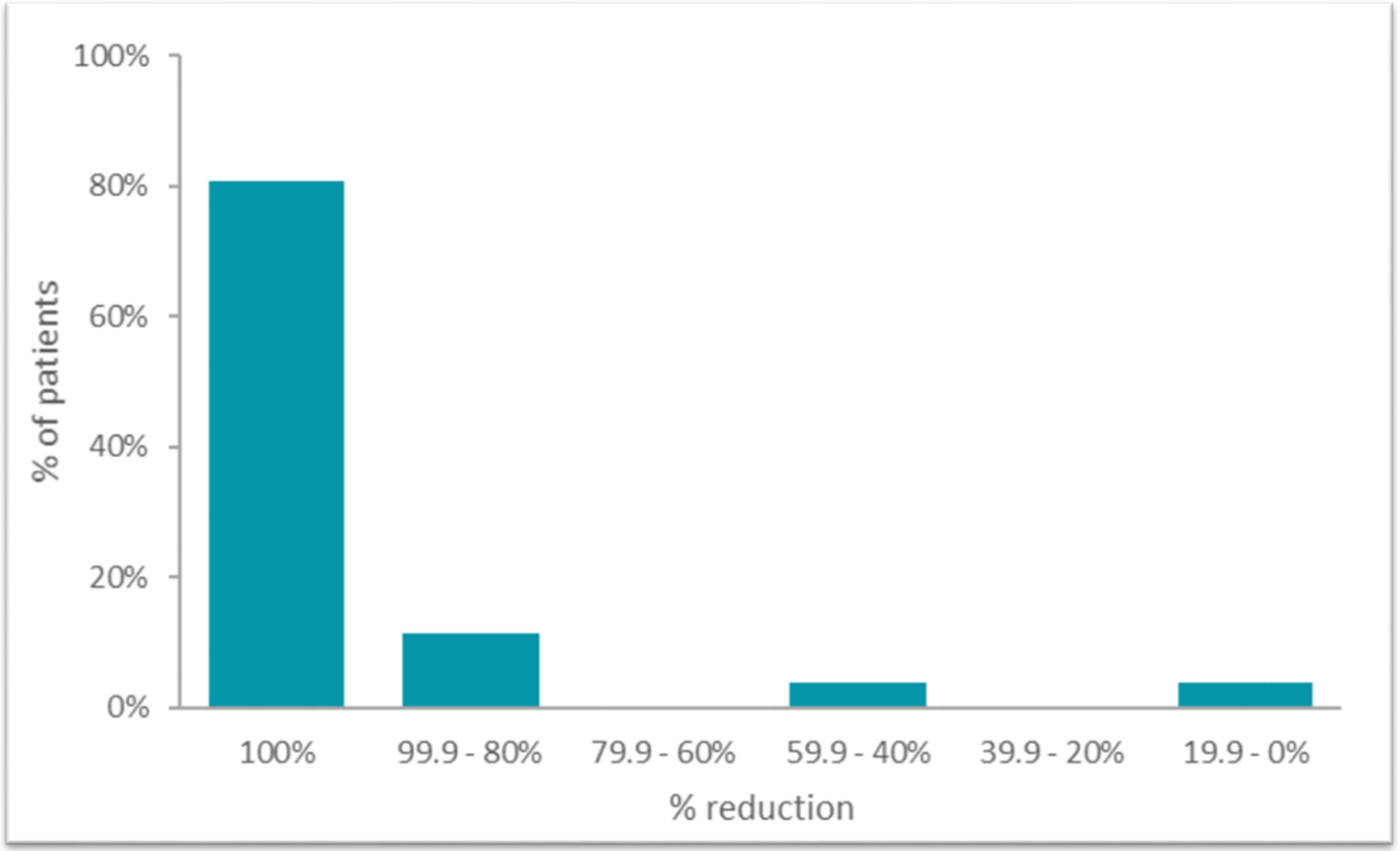
Cumulative ascites (L) drained by paracentesis:



* *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

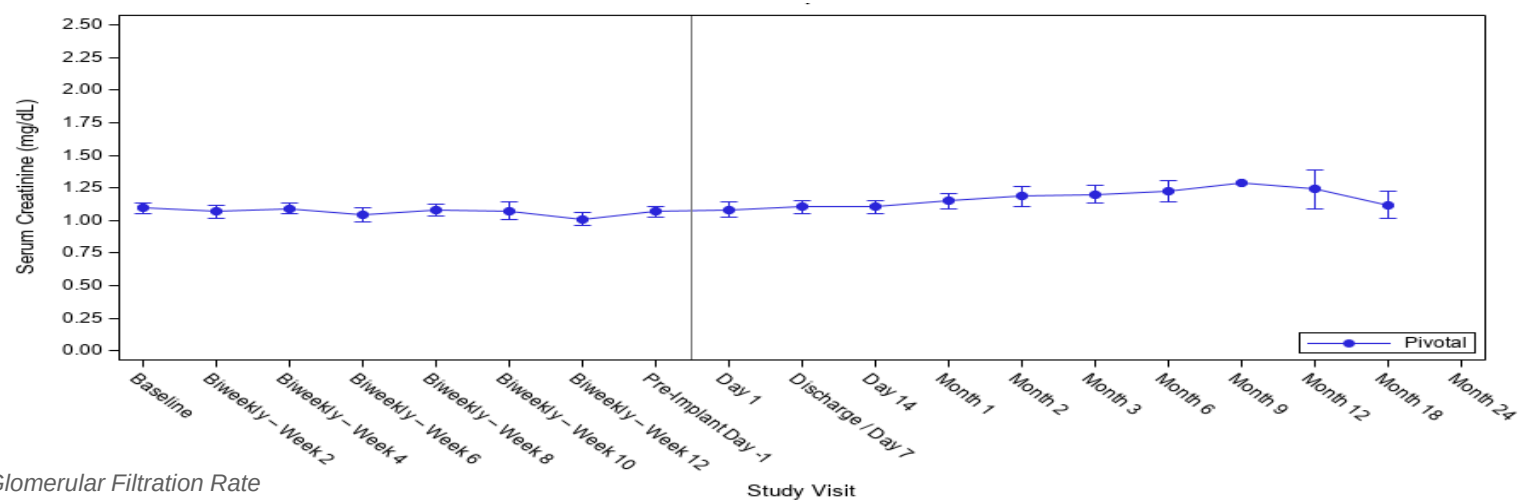
- **AKI events post-implant were manageable**

	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

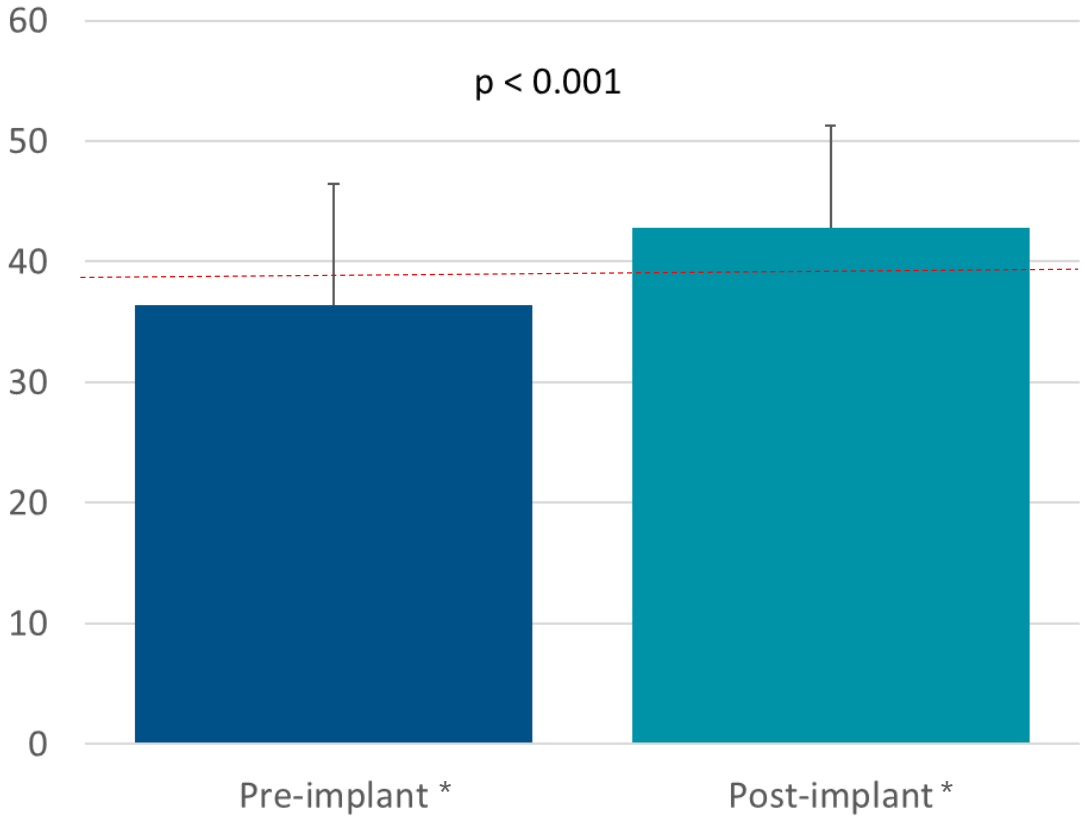
- Ascites Q:
  - Specific health-survey questionnaire for ascites
  - Endpoint: improvement* in Ascites-Q Score
  - Subdomains of Ascites-Q: abdominal fullness, lack of appetite, early satiety, nausea, abdominal pain, back pain, short of breath

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

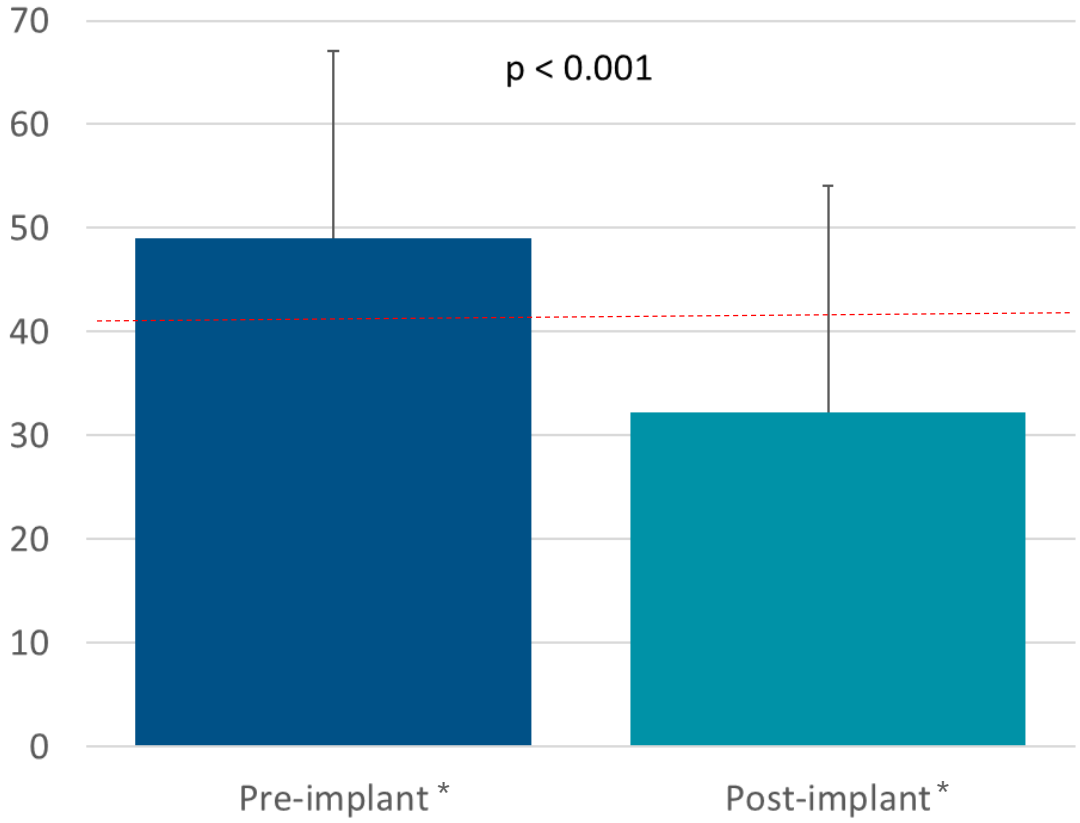
Therefore any reduction in QoL benefit over time may well be due to advancement of underlying disease rather than decline in alfapump benefit.

POSEIDON: Clinically meaningful and statistically significant improvement in QoL

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



Ascites Q Score (lower is better):



QoL: *Quality of Life*

* *Pre-implant = at baseline; Post-implant = at 6 months post-implantation*

SF-36 Physical Component Score is an independent predictor of mortality[1]

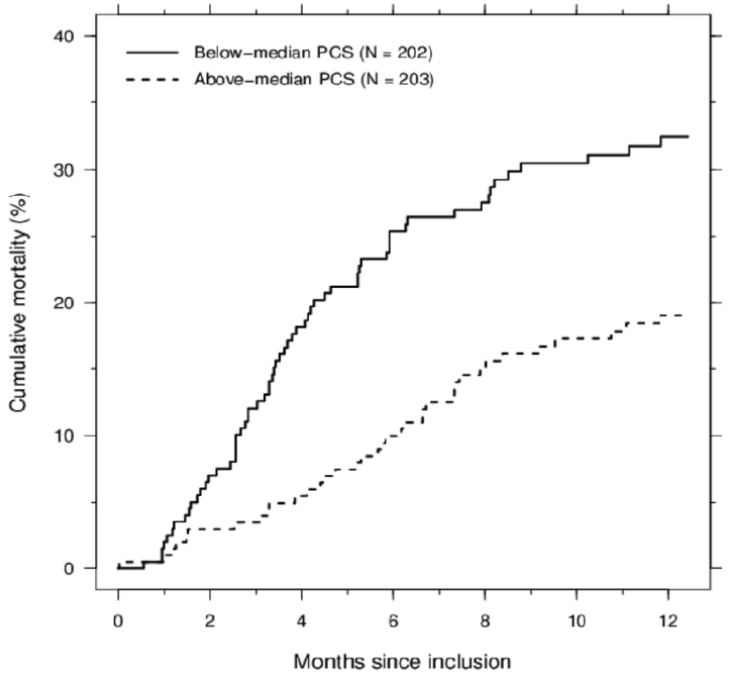
Multicenter randomized controlled study in patients with recurrent (N=164) and refractory (N=241) ascites

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)

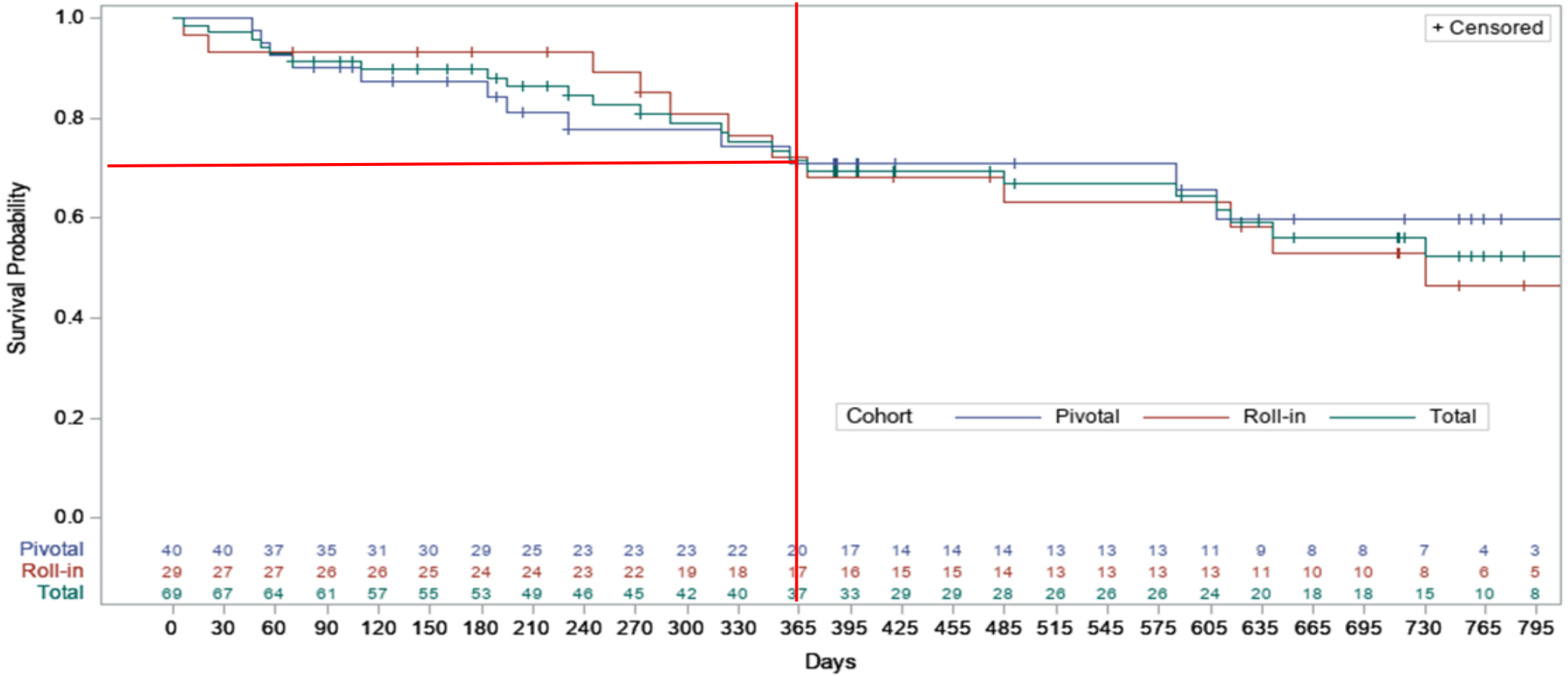


A higher physical component score in the SF-36 QoL tool predicted lower risk of death

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

POSEIDON: 70% survival at one year post-implantation

Compares favorably to published literature citing 50% survival at 1 year from diagnosis of refractory ascites(1)



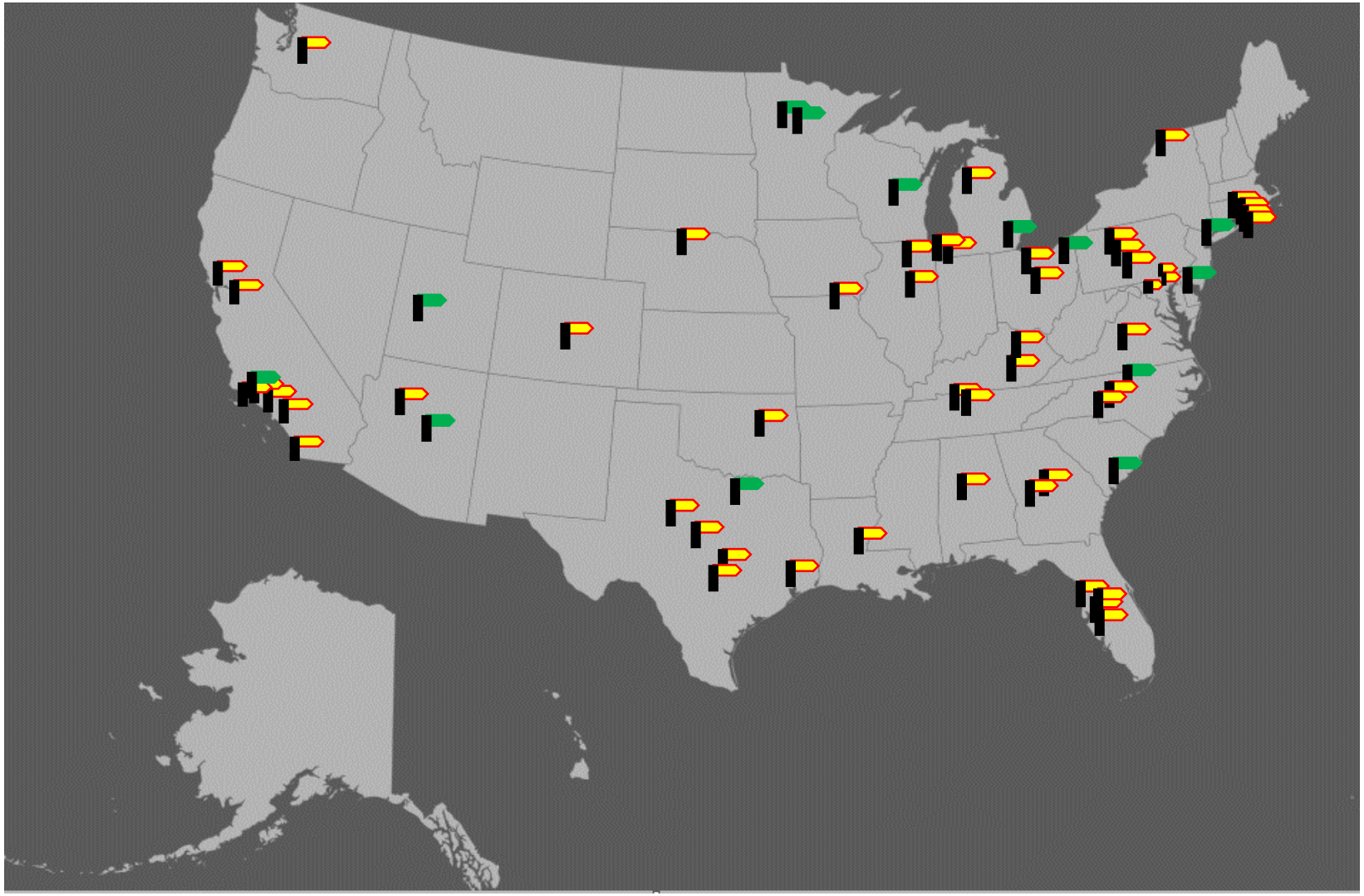
Note: POSEIDON study not powered for survival

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

Top 60 liver transplant centers (2021)

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

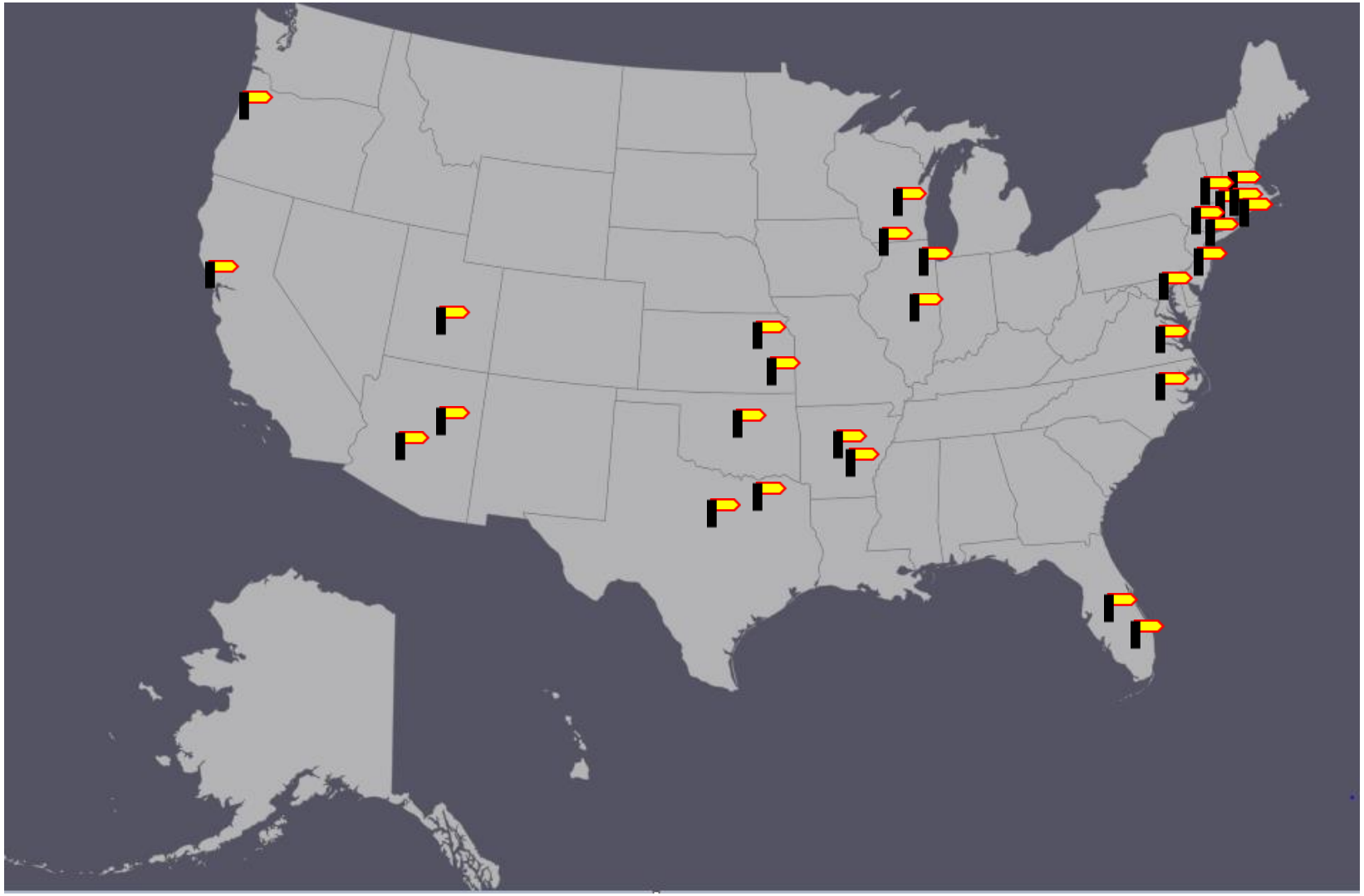
POSEIDON center (N = 13)



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)

sequanamedical

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

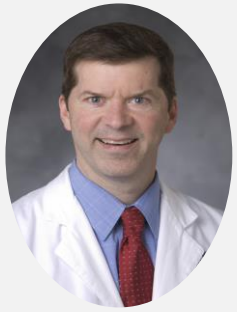
Professor of Medicine at Cleveland Clinic Lerner College of Medicine at Case Western Reserve University

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

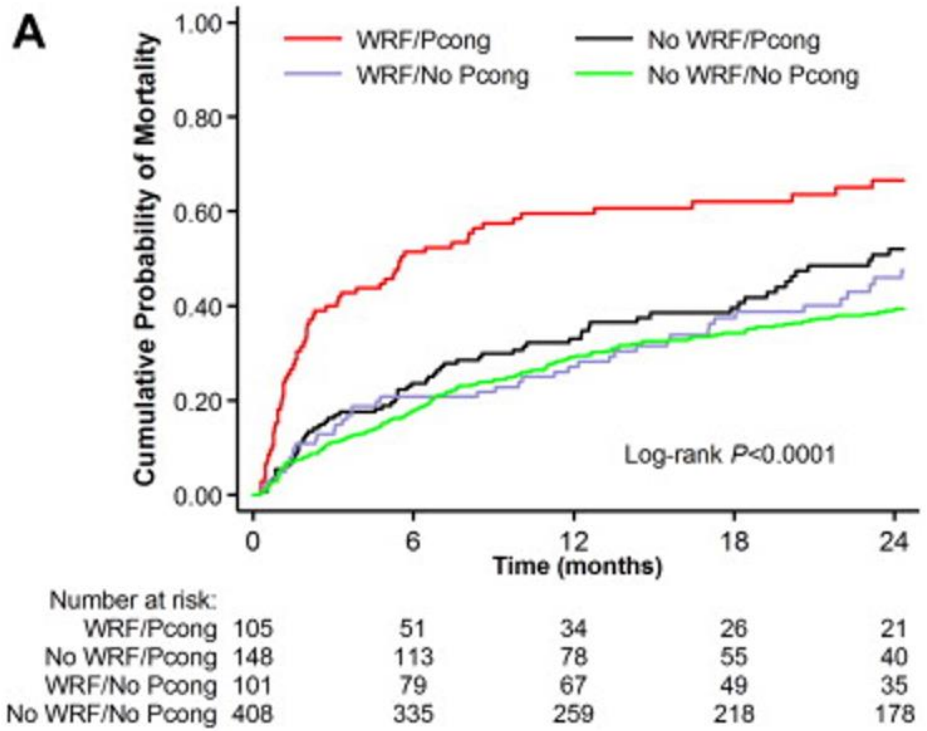
Professor of Medicine in the Division of Cardiology at Duke University School of Medicine
Director of Cardiovascular Research at the Duke Clinical Research Institute and Vice-Chief for Clinical Research in the Division of Cardiology

Dr. James Udelson

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

Persistent congestion and Worsening renal function

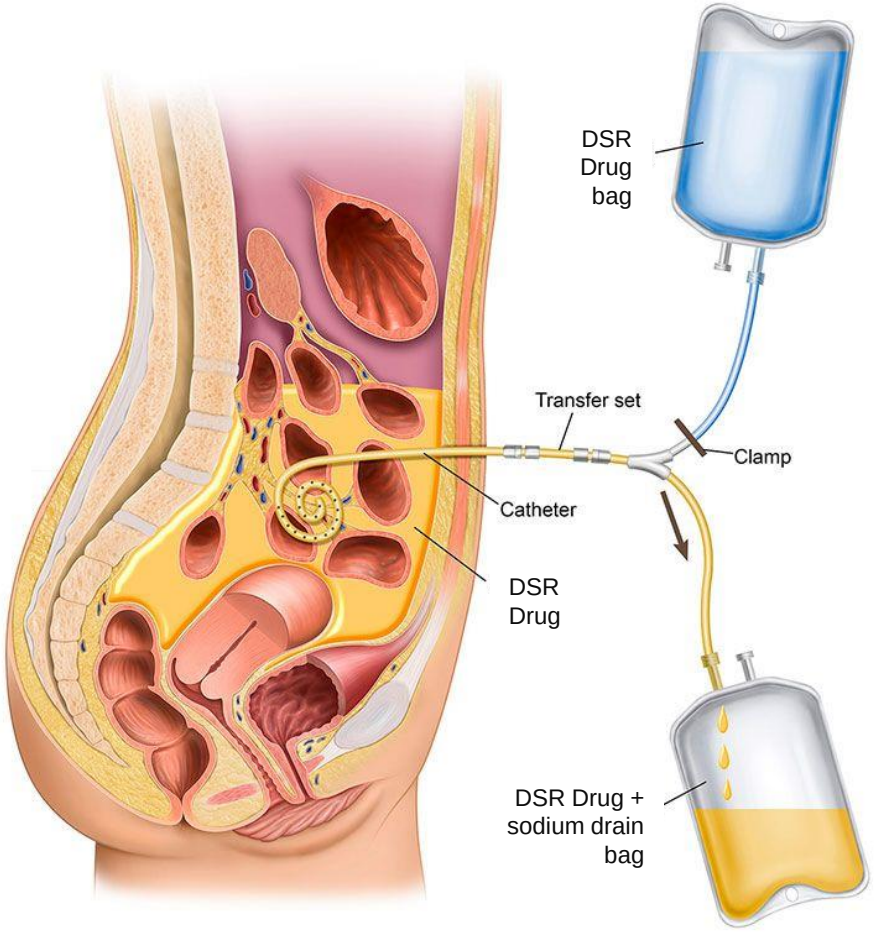
Persistent congestion and worsening renal function are key targets in decompensated heart failure



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

***WRF**: Worsening Renal Function; **ADHF**: Acute Decompensated Heart Failure; **Pcong:** Persistent Congestion*

DSR therapy treatment overview



Step 1: Peritoneal catheter placement

Step 2: DSR treatment episode

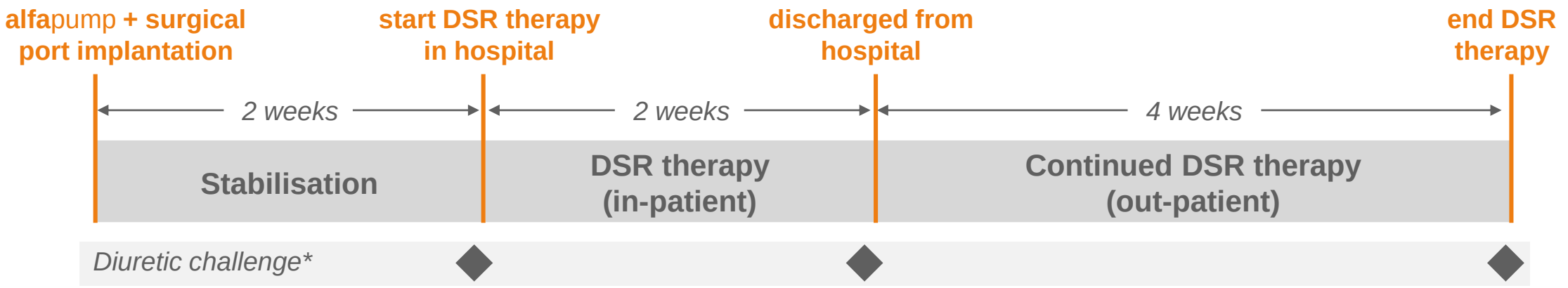
1. Infusion of DSR Drug
2. 24 hour dwell
3. Drainage

- Week 1: 5x DSR therapy
- Week 2-4: 3x/week DSR therapy

Step 3: Catheter removal

RED DESERT: The first repeated DSR therapy study

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



Study Endpoints

- **Primary:** absence/rate of device, procedure and/or therapy related serious adverse events
- **Secondary:** ability of the **alfa**pump 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: 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*

RED DESERT: Highly effective management of fluid & sodium

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

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

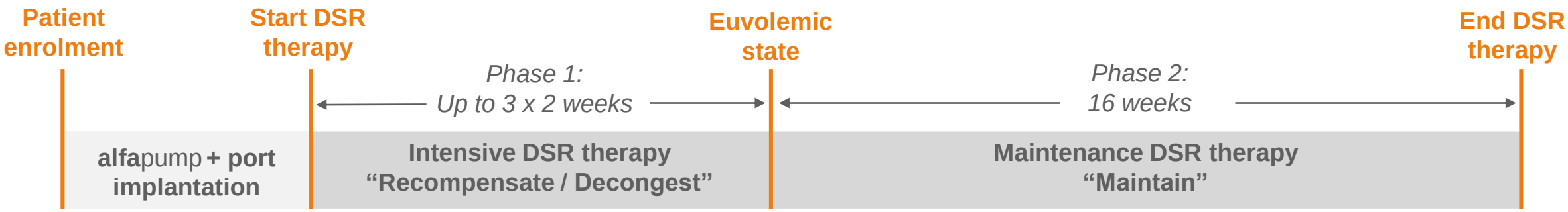
Study recruited severely ill heart failure patients on very high doses of oral loop diuretics

** in follow-up extension with DSR; † subject 101-009 died at D3*
*** loop diuretics in furosemide equivalents (mg)*

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

SAHARA: Ph. 2a in target patient population

Decompensated heart failure patients with persistent congestion on high dose diuretics



Study Endpoints

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

SAHARA: Expanding into decompensated patients

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

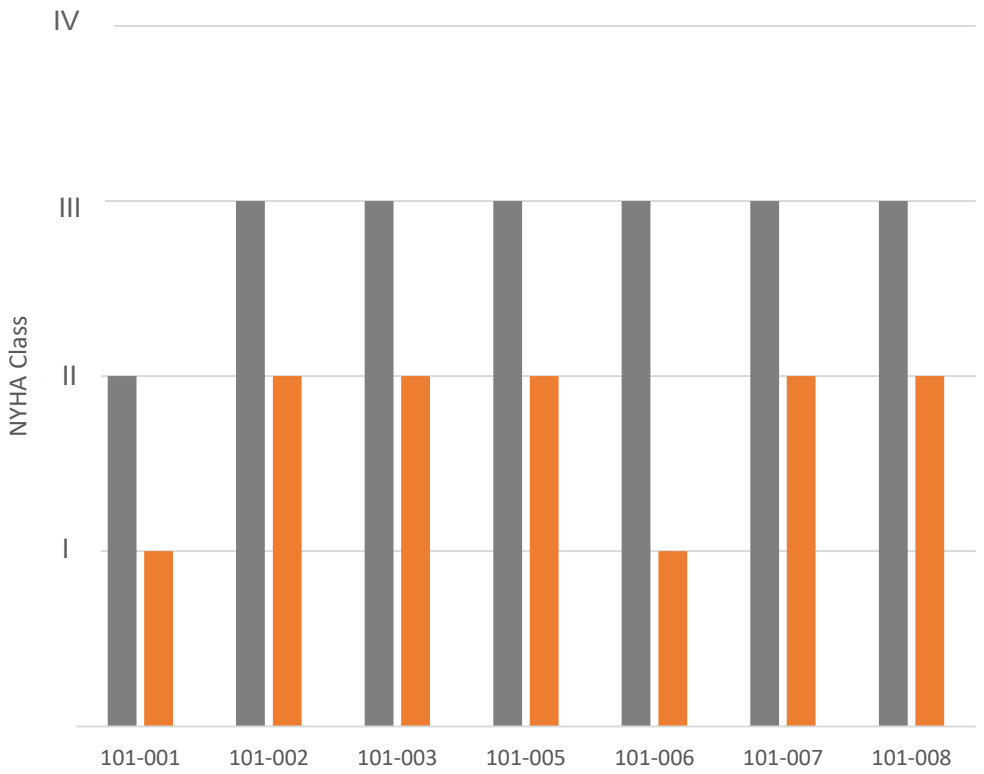
"The SAHARA results are highly encouraging and indicate the potential for DSR therapy to deliver clinically meaningful decongestion and durable improvements in cardio-renal function and thus diuretic response" – Dr. Testani, Yale

[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*

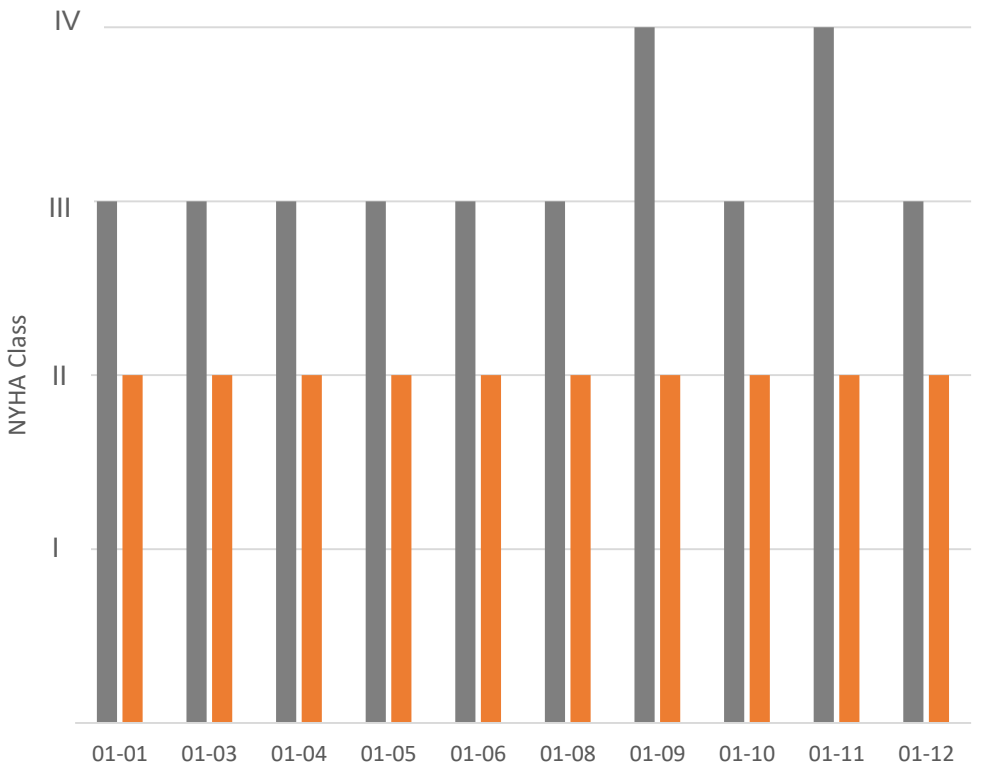
mean value; ** assessed by 6-hour excretion of sodium after IV administration of 40mg furosemide;* ***NT-proBNP**: N-terminal-pro hormone B-type Natriuretic Peptide (analysed in local lab);* ***eGFR****: estimated glomerular filtration rate*

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*

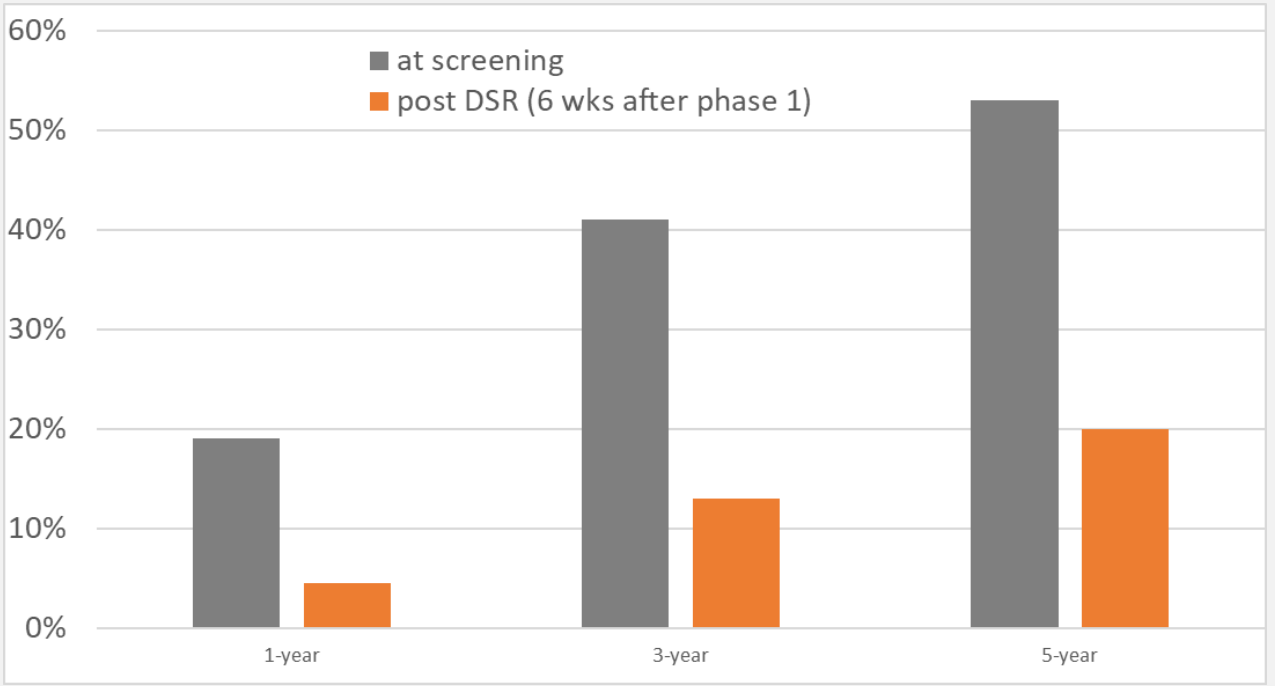
Note: data on NYHA classification collected outside study protocols of RED DESERT and SAHARA

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)*

SAHARA: Safety

No clinically relevant changes in serum sodium levels or progressive hyponatremia

- 3 SAEs in 3 patients:
  - Blocked peritoneal catheter (phase 2) — 2 in 2 patients → DMC: related to study device but unrelated to implant procedure or treatment
  - Stable angina (extension) – ongoing — 1 in 1 patient → DMC: unrelated to study device, implant procedure or treatment
- No SAEs related to implant procedure or DSR treatment

SAE: *Serious Adverse Event;* ***DMC****: Data Monitoring Committee*

Evaluating potential for DSR in renal failure

Complementary opportunity leveraging heart failure programme capabilities

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