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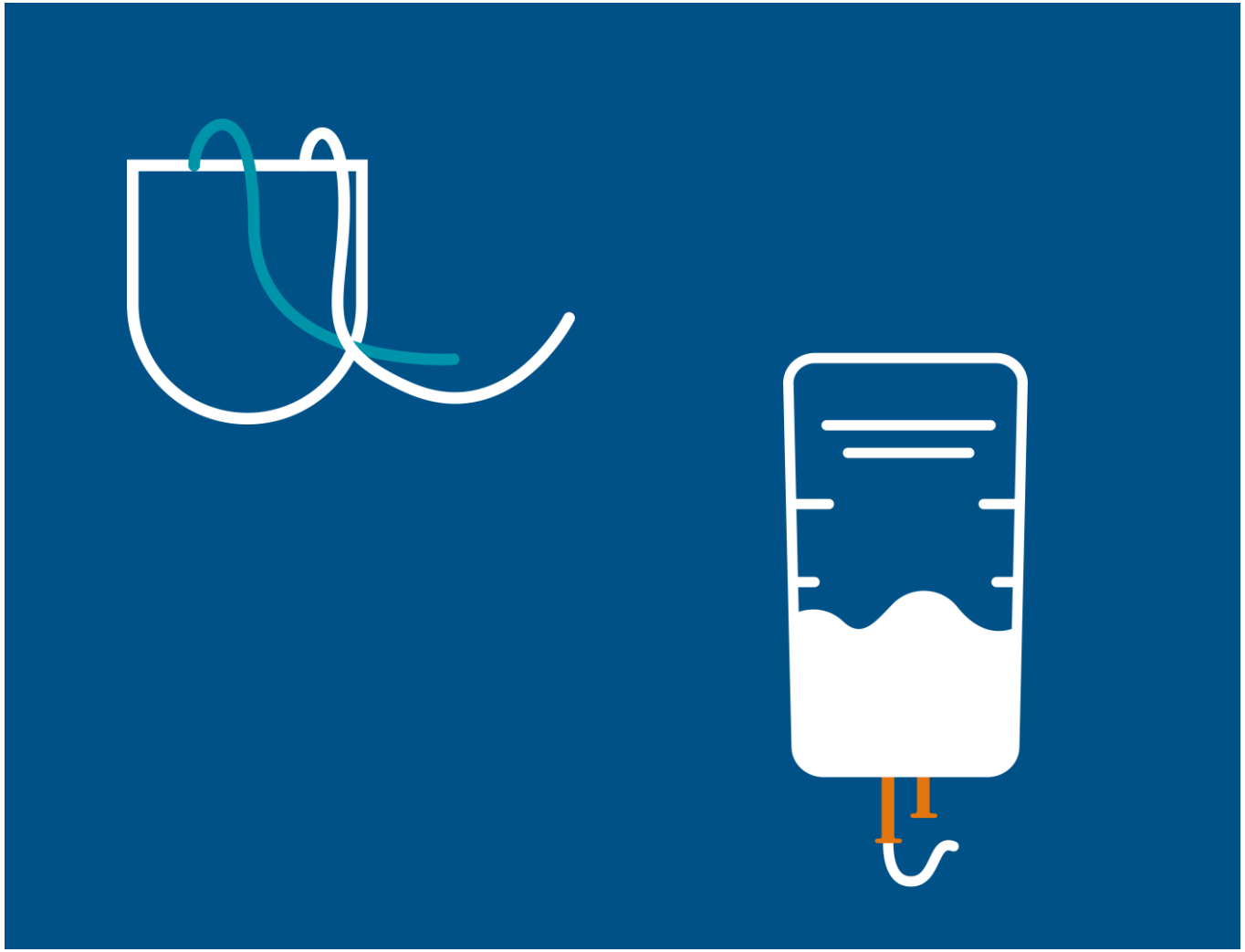

DSR®

A Disease Modifying Heart Failure Drug Therapy

Webcast presentation – 19 July 2022

Today's presenters

Ian Crosbie
Chief Executive Officer

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Disclaimers

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- DSR® therapy is still under development and it should be noted that any statements regarding safety and efficacy arise from ongoing pre-clinical and clinical investigations which have yet to be completed. DSR® therapy is currently not approved for clinical research in the United States or Canada. There is no link between DSR® therapy and ongoing investigations with the **alfa**pump® system in Europe, the United States or Canada.

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DSR – A Disease-Modifying Heart Failure Drug Therapy

Clinical proof-of-concept of Direct Sodium Removal (DSR) delivered – addressing key unmet clinical needs

Proof-of-concept in diuretic-resistant heart failure patients with DSR 1.0

- RED DESERT (completed)
  - 8 patients
  - Up to 23 months follow-up data*
- SAHARA (ongoing)
  - 12 patients enrolled
  - Up to 11 months follow-up data*

Clear improvements in validated clinical measures

- Eliminated congestion and restored euvolemia
- Improved cardio-renal health
- Restored diuretic-response
- Improved ejection fraction
- Durably and meaningfully reduced loop diuretic dosing
- Improved NYHA status by one level**

Targeting key clinical endpoints

- No congestion-related heart failure re-hospitalizations
- 75% reduction in one-year predicted mortality (calculated using Seattle Heart Failure Model)***

"We have nothing [for HF congestion] when loop diuretics don't work"

"We do what we can with sodium overloaded patients, but this is a therapy that can reduce the sodium"

"Loop diuretic reduction is dramatic – the tail is awesome"

"This is a heart failure therapy"

** Long-term follow-up data on loop diuretic dosing; ** NYHA class data collected outside study protocol; *** Predicted one-year survival analysis using Seattle Heart Failure Model with seven patients from RED DESERT and eight patients from SAHARA pre- and post-intensive DSR therapy. Analysis includes physician-assessed data collected post hoc.*

***NYHA**: New York Heart Association*

Focus: Short Term DSR with Proprietary DSR 2.0

Bringing important clinical benefits to a large and underserved patient pool as quickly as possible

Focus on Short Term DSR	• 3 to 4 weeks of intensive DSR delivers clinical benefits lasting 6 – 12 months • "Drug only" regulatory path – shorter and lower risk compared to "Drug-Device regulatory path for Long Term **alfa**pump DSR"
SAHARA – Key Lessons Learned	• Enrollment completed for DSR 1.0 (n = 12) ("SAHARA 1") • Extending study to gain initial insights for DSR 2.0 in humans to support MOJAVE IND ("SAHARA extension")
Expand MOJAVE	• Expanding MOJAVE to create compelling package for partnering • US Phase 1b/2a randomized, controlled study of Short Term DSR • DSR 2.0 with peritoneal catheter • DSR 2.0 pre-clinical development on track • US IND filing planned by year end
Strong granted IP	• Low or no sodium drug for the treatment of heart failure • Supports premium drug pricing based on reduction in re-hospitalization and reduction in predicted mortality
Long-term DSR potential for future development	• Future opportunity for market expansion / lifecycle management

IND: *Investigational New Drug*

Diuretic-Resistance is a Major Problem in HF Patients

Clear need to treat drug-resistant congestion in chronically congested patients (the “frequent flyers”)

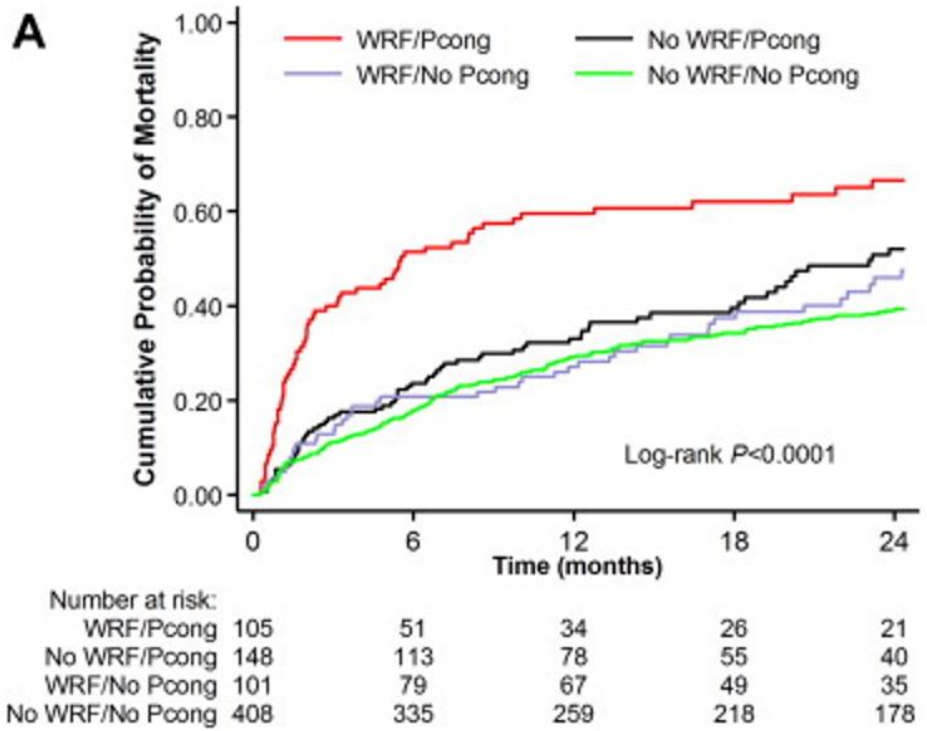
- Heart Failure (HF) is the leading cause of hospitalizations in patients over 65 in the US
  - Annual cost of $14.5 billion
- Congestion is the primary driver of morbidity and hospitalization in HF
  - 90% of US HF hospitalizations are due to congestion
- Loop diuretics are standard-of-care despite well recognized toxicity and resistance is common
  - Half of acute decompensated HF patients are discharged with no clinically relevant loss of weight
  - One in four are re-admitted within 30 days of discharge
  - There is no apparent successor to loop diuretics in development
- Few effective treatments for chronically decompensated / congested patients

Source 1: Most Frequent Principal Diagnoses for Inpatient Stays in U.S. Hospitals (2018) Kimberly W. McDermott, Ph.D., and Marc Roemer; Source 2: Fluid Management in Patients with Chronic Heart Failure Pierpaolo Pellicori, Kuldeep Kaur and Andrew L Clark (2015)

***HF:** Heart Failure; **CHF:** Congestive Heart Failure*

Eliminating Congestion While Protecting Kidney is Key

Persistent congestion and worsening renal function predict reduced survival



Source: 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*

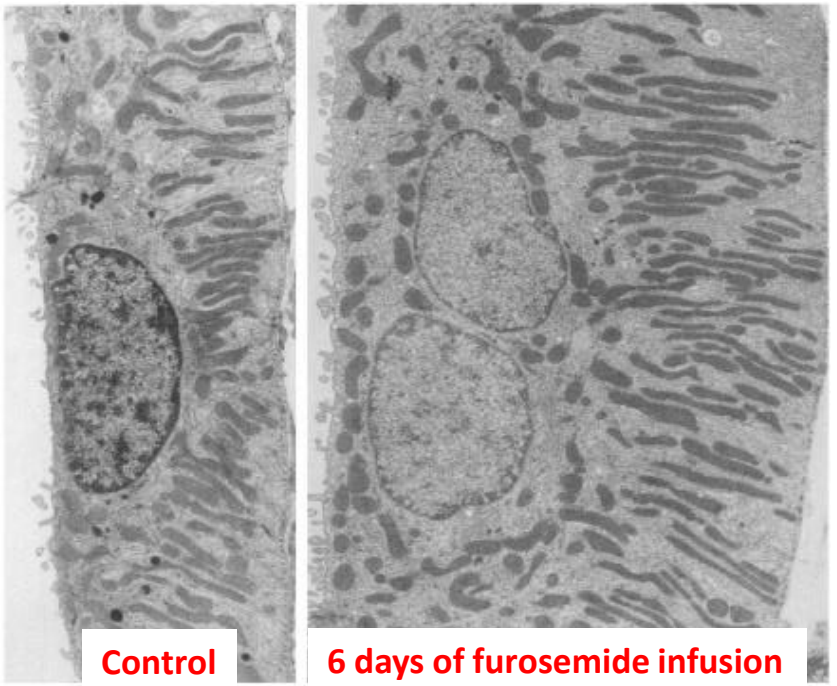
Current Standard of Care is BAD for the Kidneys

And resistance is common

- Fluid overload is initially treated with diuretics
- Loop diuretics strongly activate the neurohormonal system
  - Leads to increased sodium retention
  - Blocking of neurohormones is mainstay of HF therapy (ACE-inhibitors / MRA / ARB / beta-blockers)
- Over time, kidneys become less and less responsive to loop diuretics
- Continuous exposure of the kidney to loop diuretic causes massive structural remodeling
- Escalating doses required to maintain fluid balance are a double-edged sword

“Save the heart or save the kidney”

Distal tubular cells



Source: Kaissling B Am J Physiol. 1985 :F374-81.

ACE: *Angiotensin-Converting Enzyme;* ***MRA:*** *Mineralocorticoid Receptor Antagonists;* ***ARB****: Angiotensin Receptor Blocker*

DSR Tackles the Key Challenge of Sodium Overload

Sodium overload drives heart failure – and there are limited treatment options today

- Primary pathophysiologic driver of water accumulation is sodium retention, with fluid largely passively following the retained salt.[1, 2]
- Estimated 200,000 chronically congested HF patients in the US (“frequent flyers”)
  - Consume large amount of clinical resources and have poor clinical prognosis
  - Long length of stay with high intensity of care – major cost burden for hospitals, especially under risk sharing mechanisms
- Clinical guidelines rely on diuretics for congestion – no clear guidance for patients with diuretic-resistance
- DSR tackles key unmet need of sodium overload when diuretics are no longer effective
- Most HF therapies / treatments are focused on “structural heart” – DSR is complementary to GDMT therapies

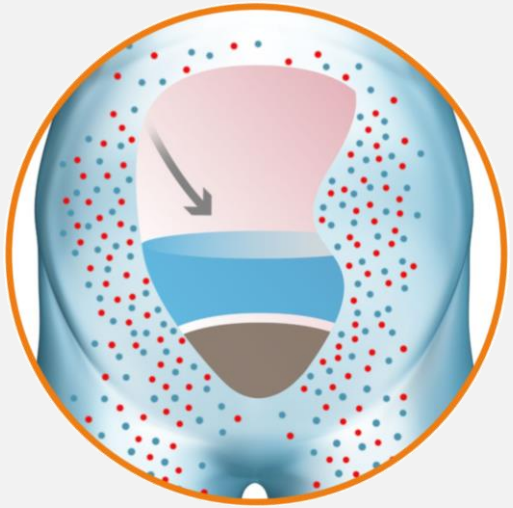
Source 1: Guyton AC and Hall JE. Textbook of medical physiology. Philadelphia: Saunders; 2000. ; Source 2: Brenner BM and Rector FC. Brenner & Rector's the kidney. Philadelphia: Saunders Elsevier; 2008.

***GDMT:** Guideline Directed Medical Therapy*

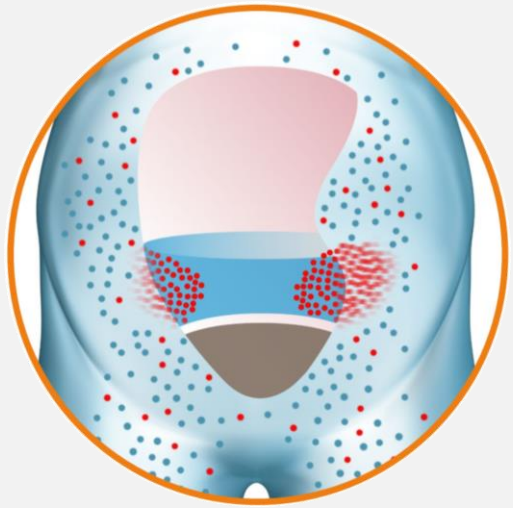
Direct Sodium Removal (DSR)

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

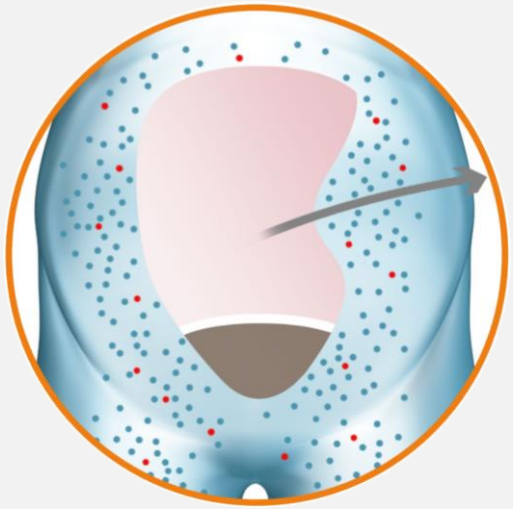
1 Sodium-free DSR product administered to peritoneal cavity



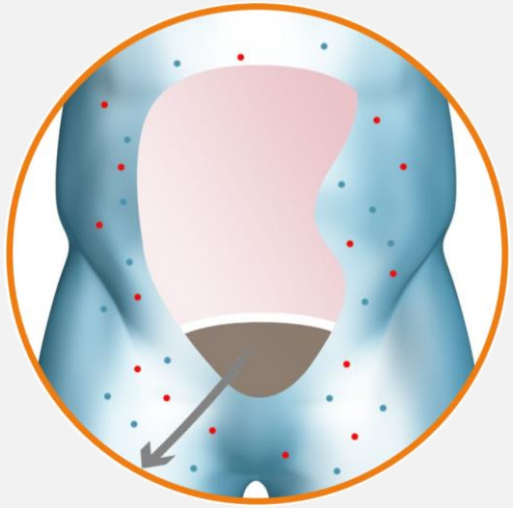
2 Sodium diffuses from body into DSR product



3 DSR product + extracted sodium removed from the 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 the US and Europe

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

- End of 6-week study: over 150% increase** in diuretic response***

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 I (Interim): DSR Tackles Congestion

10 evaluable decompensated diuretic-resistant HF patients on intensive DSR therapy[1]

Safely, effectively and rapidly eliminate persistent congestion & restore euvolemia

- Weight loss* of ~6kg vs. baseline
- 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: more than doubling* to near normal levels

No congestion-related heart failure re-hospitalizations

"These interim results are highly encouraging and could potentially provide a course of therapy for severely ill diuretic-resistant heart failure patients with persistent congestion where alternative treatment options are currently exceedingly limited" – Dr. Testani, Yale

Note: SAHARA I = SAHARA study using DSR 1.0

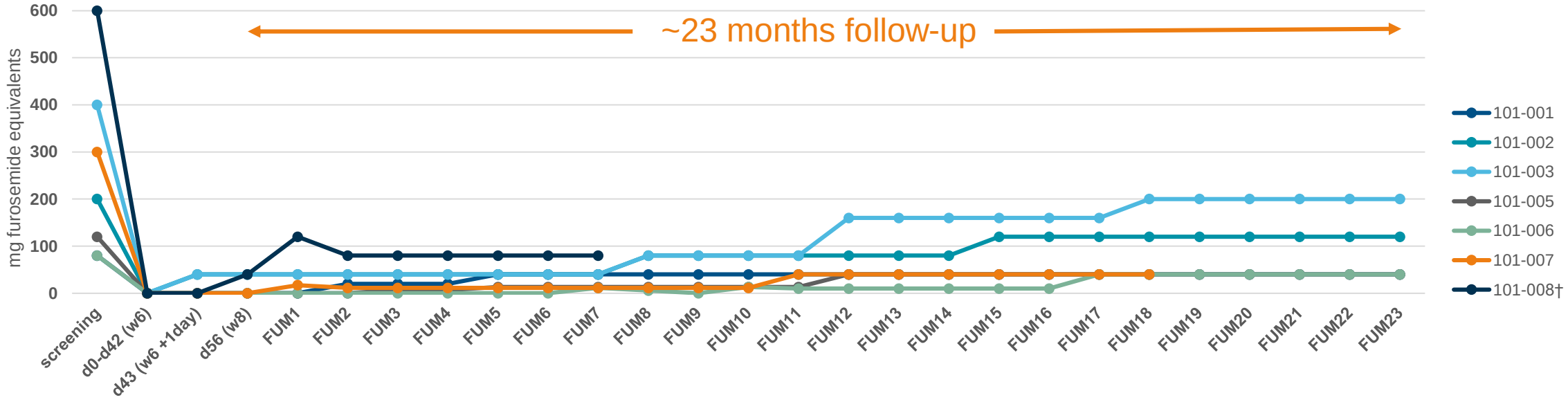
[1] two additional patients were enrolled but one patient died due to a cardiac arrest three days after study initiation and for one patient the study protocol was not correctly applied

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*

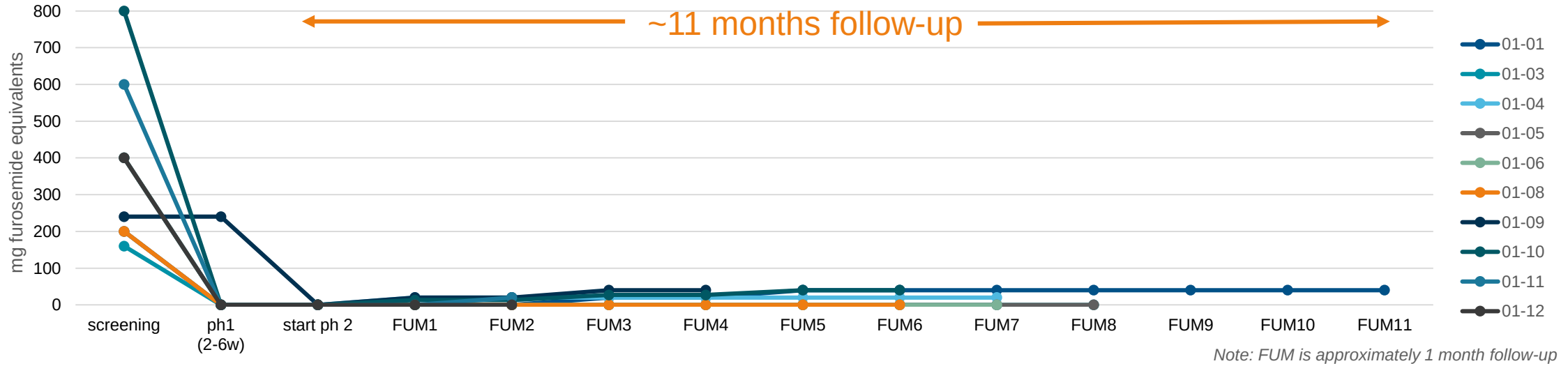
Long-Term & Major Reduction in Loop Diuretic Dosing

Clear demonstration of improvement in cardio-renal health – driving improved clinical outcomes

RED DESERT



SAHARA I



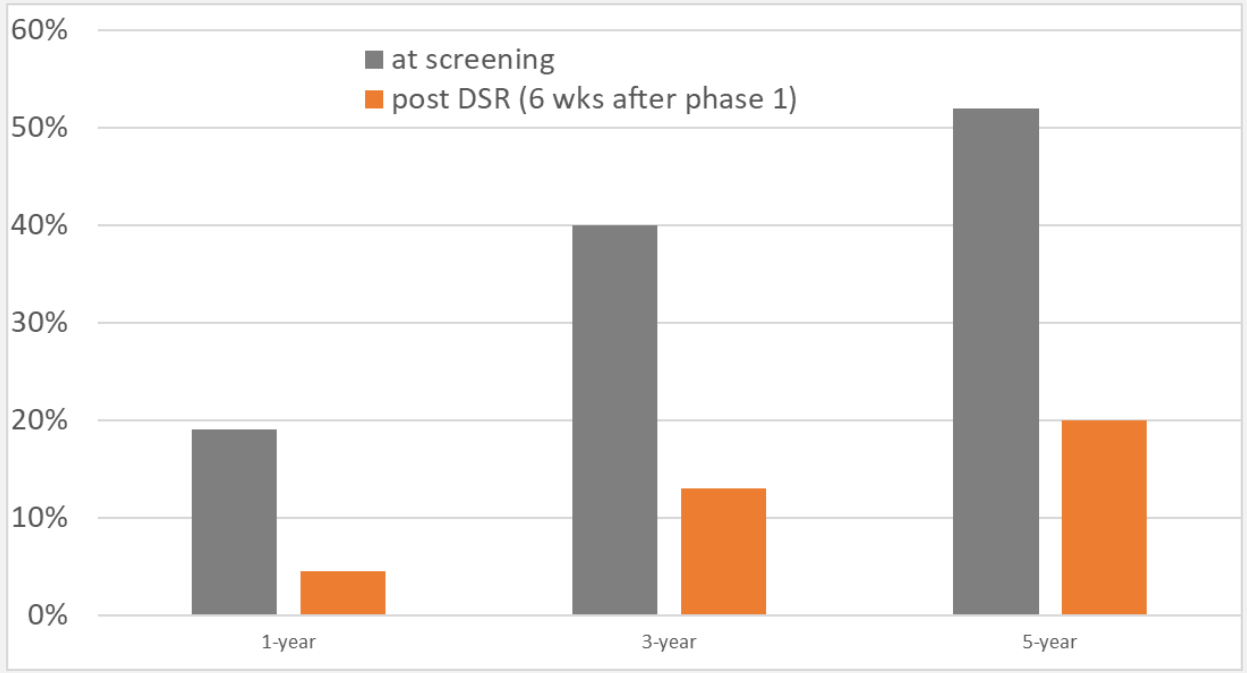
Note: FUM is approximately 1 month follow-up

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 90.5% vs. 88.5% respectively

- Substantial reduction in overall predicted mortality post DSR* vs. screening, at 1, 3 and 5 years



** Predicted one-year survival analysis using Seattle Heart Failure Model with seven patients from RED DESERT and eight patients from SAHARA I 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)*

Moving to Proprietary DSR 2.0

Improved clinical and safety profile driving high margin recurring revenue stream

DSR 1.0
Sodium-free D10% (off-the-shelf)

- ✓ Clinical proof-of-concept
- ✓ Rapid clinical path
- ✗ Therapeutic profile / Ease of use
- ✗ Safety profile

RED DESERT & SAHARA I

DSR 2.0
Sodium-free dextrose / icodextrin (proprietary)

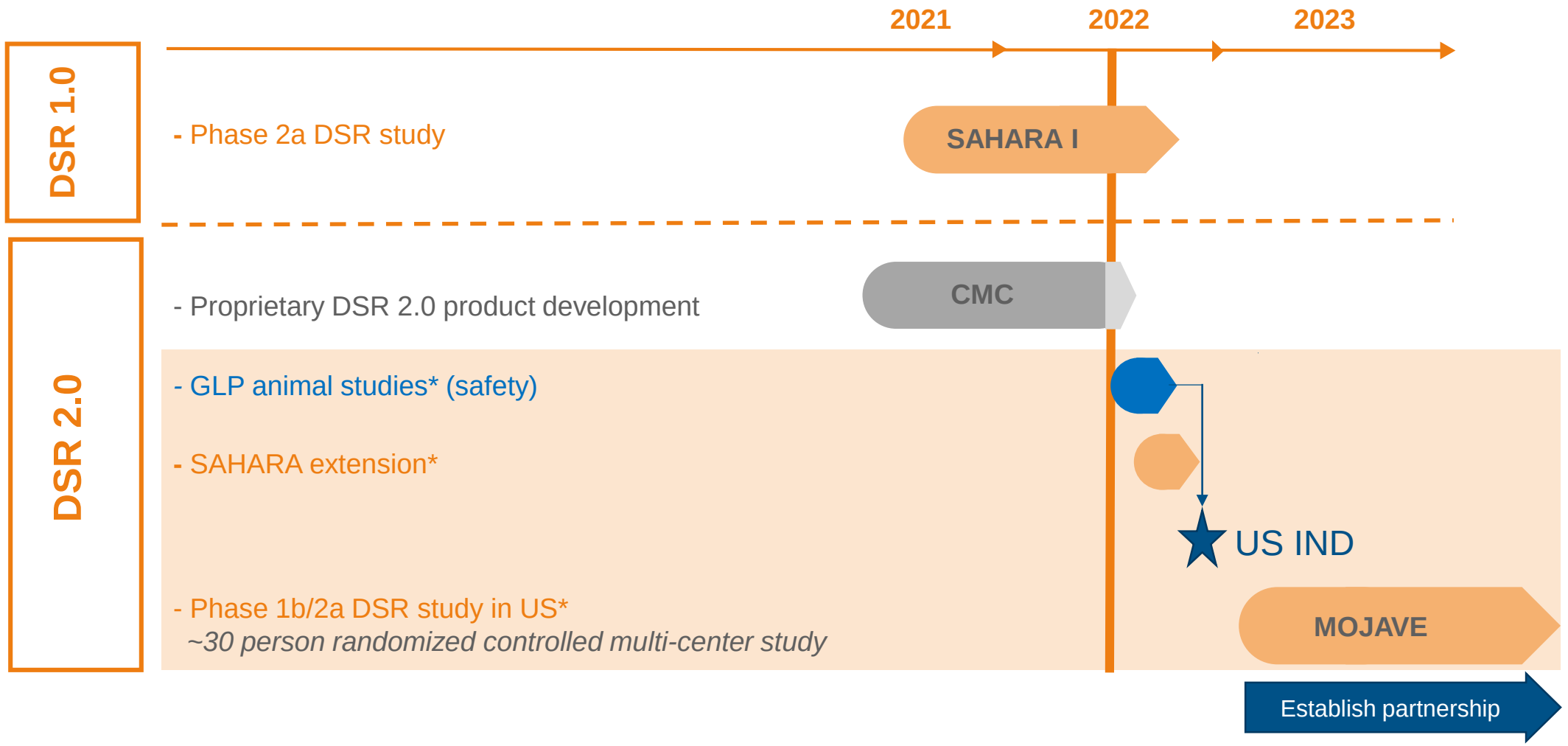
- ✓ Improved therapeutic profile
- ✓ Favorable safety profile
- ✓ Strong granted IP position in US & Europe
  - "Low or no sodium drug for the treatment of heart failure"
  - IP protection drives recurring revenue from high gross margin consumable
- First-in-human insights through extension of SAHARA with a small number of patients to support US IND
- US IND filing planned by year-end

SAHARA EXTENSION & MOJAVE

Note: SAHARA I = SAHARA study using DSR 1.0; SAHARA extension = SAHARA study using DSR 2.0

MOJAVE as Package for DSR Partnering

Leveraging the strengths of established HF player to realise commercial potential of DSR



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

** Description and timing of these studies are subject to change and/or feedback from applicable regulatory authorities*

Multi-Billion Market Opportunity

Delivering value through reduced hospitalization and improved survival

- ~400,000 HF patients hospitalized per year in the US and EU (“frequent flyers”)
  - High cost patients with major burden on healthcare systems, payors and patients

- Value based pricing of DSR drug driven by:
  - ⇨ Reduction in re-hospitalization ~$40,000 annual HF hospitalization cost per patient
  - ⇨ Increase in survival (gain in quality-adjusted life-year, “QALY”)

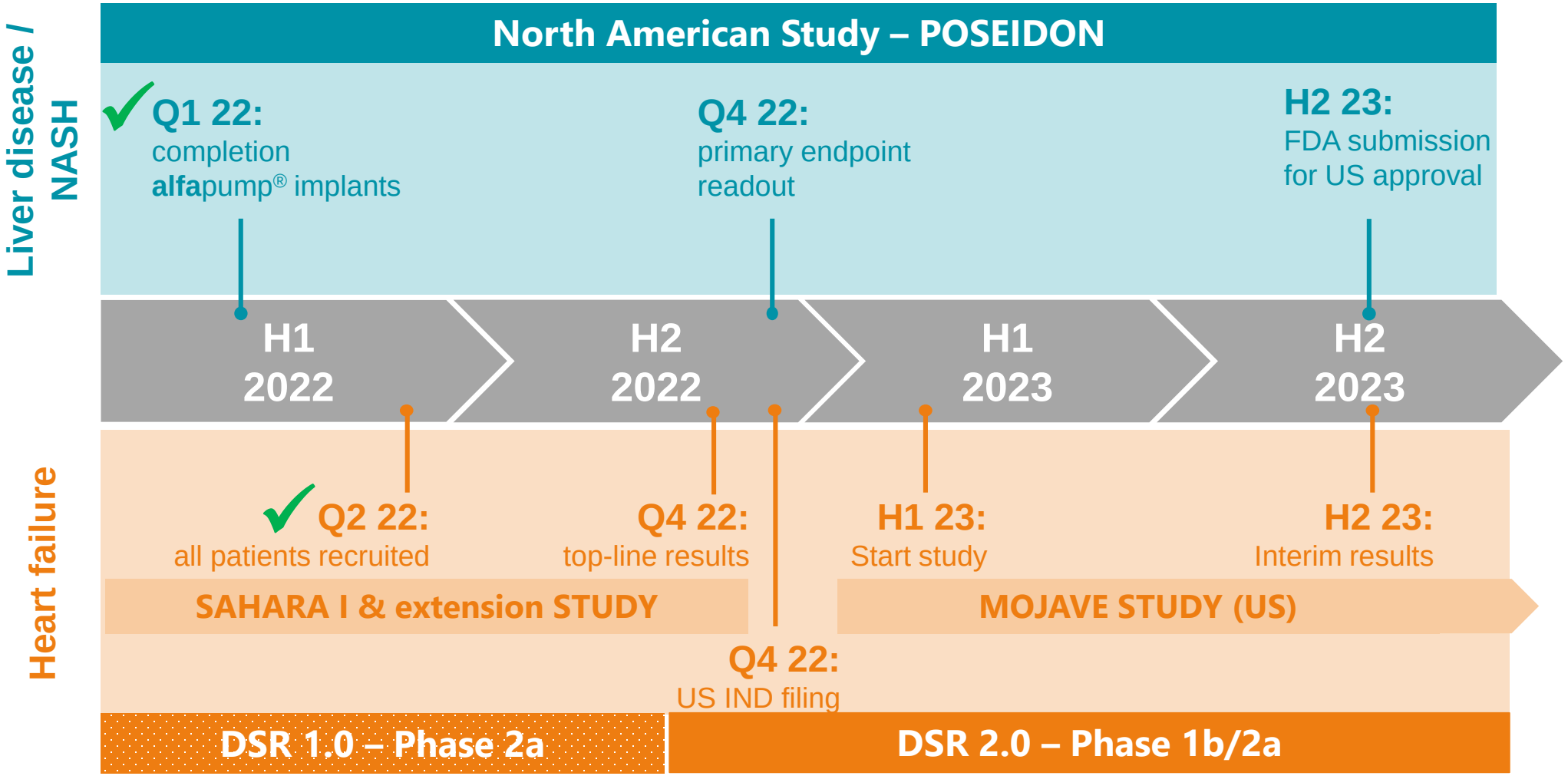
DSR: Disease-Modifying HF Drug for Key Needs

Directly targeting sodium overload, complementary to existing guidelines

- HF is the leading cause of hospitalizations in patients over 65 in US
- Congestion is the primary driver of morbidity and hospitalization in HF patients
- Loop diuretics are standard-of-care despite well recognized toxicity and resistance is major problem
- Diuretic-resistant HF is a major clinical problem with limited treatment options
- In clinical studies, DSR has been shown to safely, effectively and rapidly:
  - Decongest / recompensate diuretic-resistant HF patients
  - Meaningfully improve their cardio-renal status
  - Durably restore diuretic sensitivity of the kidney, resulting in dramatically lower diuretic needs
- **No congestion-related HF re-hospitalizations during study follow-up**
- **75% reduction in one-year predicted mortality***
- Complementary to GDMT therapies – tackling key unmet need of sodium overload
- Strong granted IP position in US & Europe
- Preparing to file US IND of DSR 2.0 by year-end & commence US efficacy study (MOJAVE)

** Predicted one-year survival analysis using Seattle Heart Failure Model with seven patients from RED DESERT and eight patients from SAHARA pre- and post-intensive DSR therapy. Analysis includes physician-assessed data collected post hoc.*

Strong Outlook for Value Drivers



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