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Euronext: SEQUA.BR

BioCapital Europe – 10 March 2022

Ian Crosbie, CEO

Innovators in the treatment of diuretic-resistant fluid overload

liver disease | malignant ascites | heart failure

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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 cirrhosis. For more information regarding the POSEIDON clinical study visit www.poseidonstudy.com.
- 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.

COVID-19 disclaimer:

- Sequana Medical is closely following the evolution of the COVID-19 global health crisis and is in constant dialogue with its partners to assess the impact and adapt 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® is a registered trademark. DSR® and **alfa**pump DSR® are registered trademarks in the Benelux, China, the EU, United Kingdom, and Hong Kong.

Uniquely positioned in two large markets

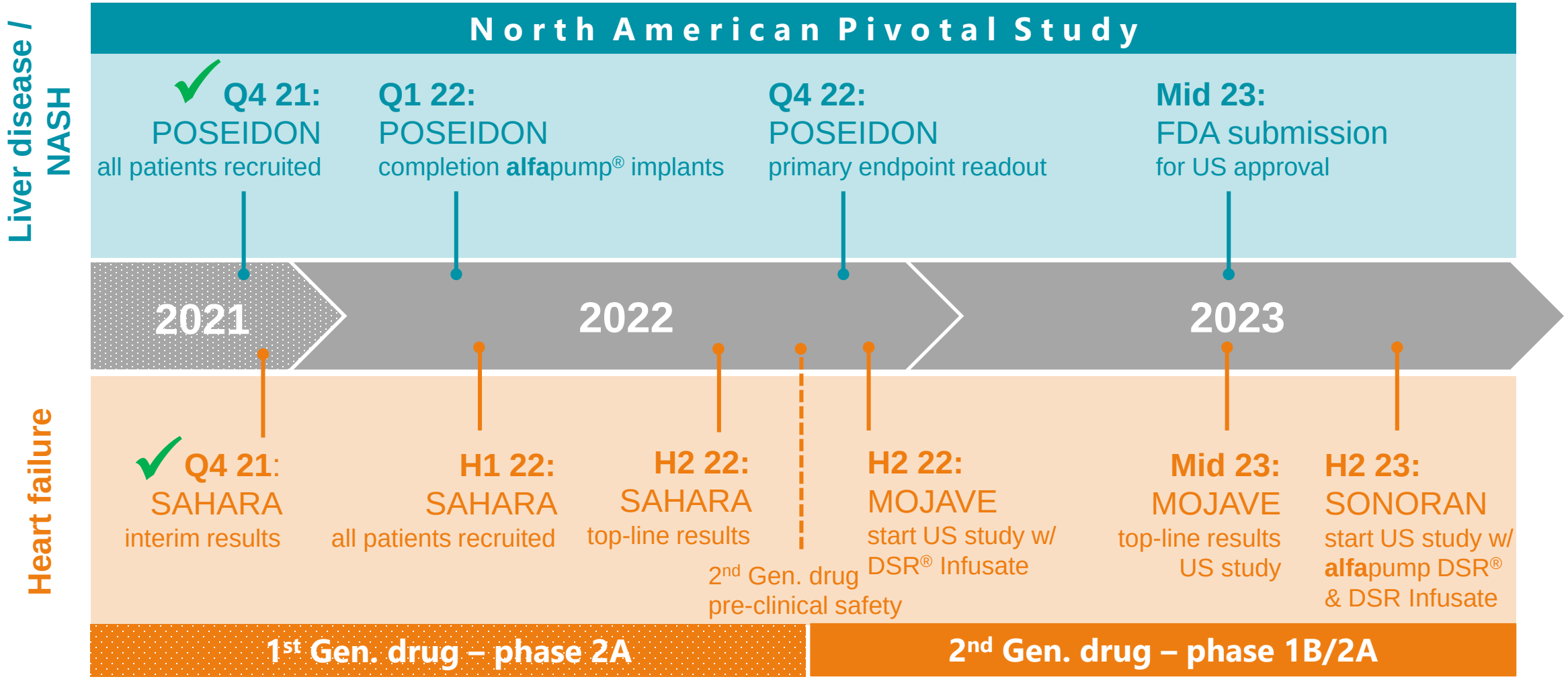
- **alfapump® in liver disease – over €3 Bn / year** (1)
  - NASH changing liver cirrhosis market and driving growth
  - Approved in EU / FDA breakthrough designation in US
  - US pivotal study fully enrolled / positive interim data / primary endpoint Q4 ‘22
  - Direct commercialisation in US

- **DSR® in heart failure – over €5 Bn / year** (2)
  - Clinical proof-of-concept established
  - Ph. 2A 1st Gen. drug – positive interim data
  - Low-risk proprietary 2nd Gen. drug – in development
  - Partnering after US efficacy study

- **Proprietary technologies treating diuretic-resistant fluid overload**
  - Key clinical problem in liver disease, heart failure, renal failure and cancer
  - Diuretic-resistance is common – alternatives have significant disadvantages
- **Strong granted IP portfolio**

Source 1: Management estimate in US within 10-20 years, that is inclusive of estimated growth in prevalence of NASH for the US based on GlobalData Epidemiology Forecast to 2026
Source 2: Management estimate in US & EU by 2026 based on GlobalData Heart Failure Epidemiology Forecast to 2026; Costanzo et al. (2007). Kiglore et al (2017)

Strong outlook for value drivers



Note: Presented timelines are subject to further developments related to the COVID-19 pandemic

alfapump®

Proven step change in the treatment of liver refractory ascites

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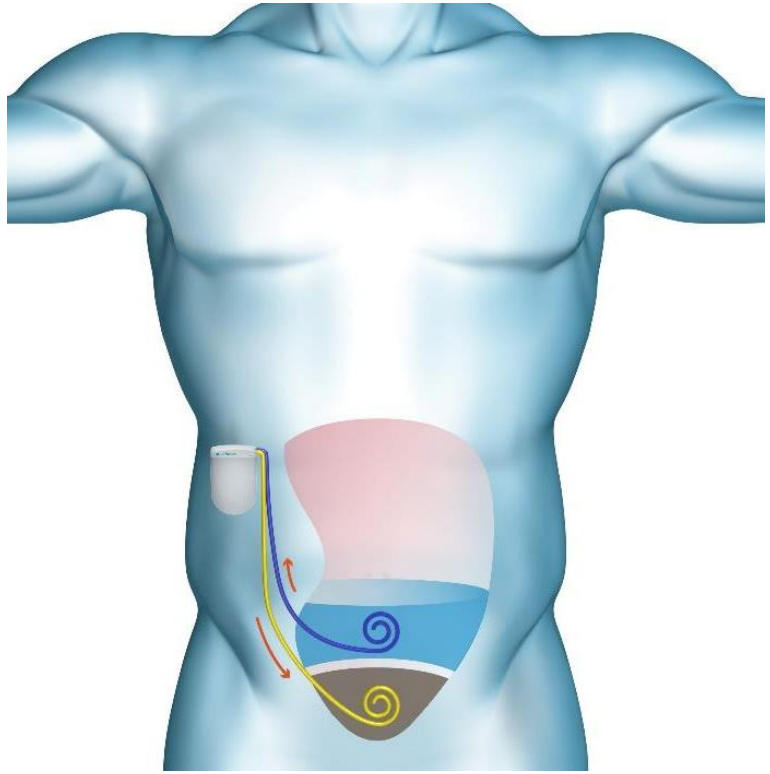
alfapump®

Eliminating fluid from the peritoneal cavity – working in partnership with the bladder

- Fully implanted
- Automatic operation
- Wireless battery charging
- Settings wirelessly adjusted
- Remote data monitoring



- Easy implantation
- Long-term implantation & catheter patency
- Moves up to 4 litres / day
- Virtually non-clogging
- No significant heating during charging and operation

Proven capabilities – over 900 systems implanted
Strong IP barriers through extensive patent portfolio & know-how

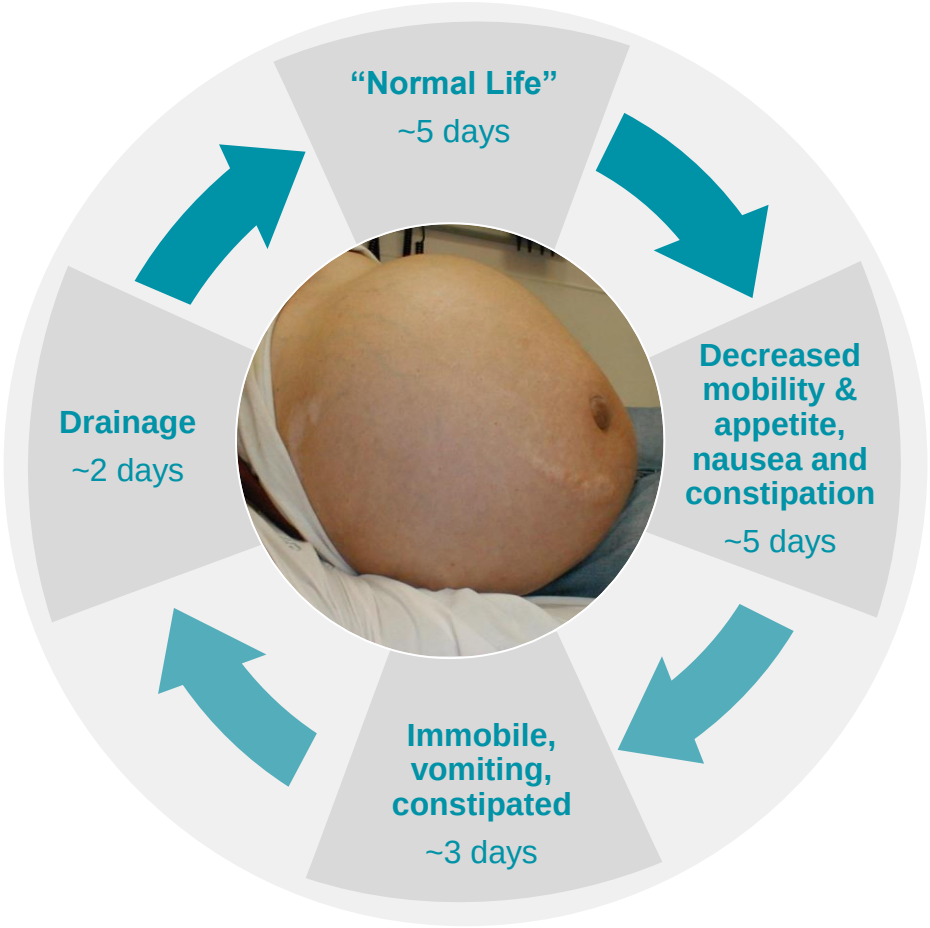
Refractory ascites – key complication of liver cirrhosis

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

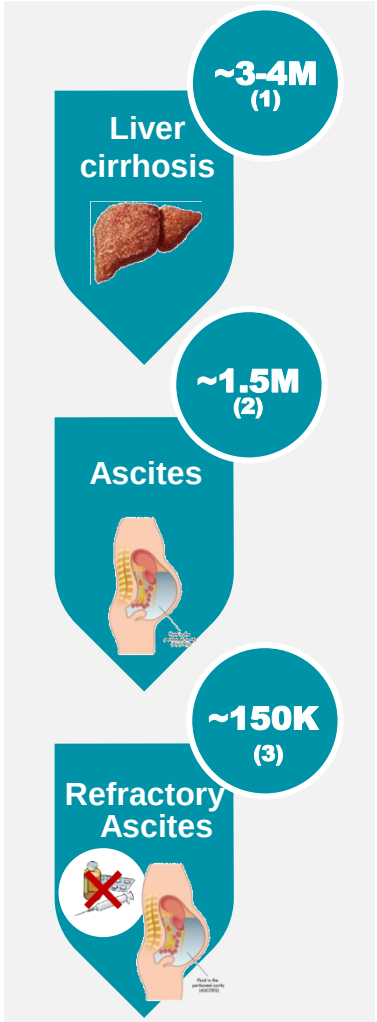
Viral infections (Hepatitis B & C)

Alcoholic Liver Disease

Non-Alcoholic Steatohepatitis (NASH)



Typical patient life[4]



Note : Prevalence of NASH in US is expected to increase by 63% between 2015-2030; Estes et al., 2018

Source 1 Management estimate in US based on Estes et al; GlobalData Nash Epidemiology Forecast to 2026; Noureddin et al., 2013
Source 2: Runyon 2009: approximately 50% of cirrhotic patients develop ascites within 10 years of diagnosis of cirrhosis
Source 3: Ginès et al., NEJM 2004: refractory ascites occurs in 5-10% patients with ascites
Source 4: Presentation of Dr. Rajiv Jalan at EASL in 2018, Large Volume Paracentesis (LVP) treatment cycle for refractory ascites

NASH transforming the face of liver cirrhosis

In US, liver cirrhosis is transitioning to a mainstream disease requiring modern treatment options

alfapump® market potential	**> €3 Bn / year**
Underlying disease	**NASH**
Patient characteristic	**“Mainstream”**

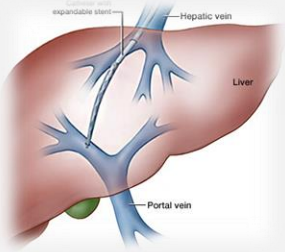
Notes: forecast US Liver market: Management estimate that is inclusive of estimated growth in prevalence of NASH for the US based on GlobalData Epidemiology Forecast to 2026.

Limitations of existing therapies

Drainage ("Large Volume Paracentesis / LVP")

Painful, Poor Quality of Life, Short Term Benefit

Transjugular Intrahepatic Portosystemic Shunt (TIPS)



Complications, Contraindications

Permanent Catheter System

External Catheter, Risk for Infections / Blockage

Liver transplantation

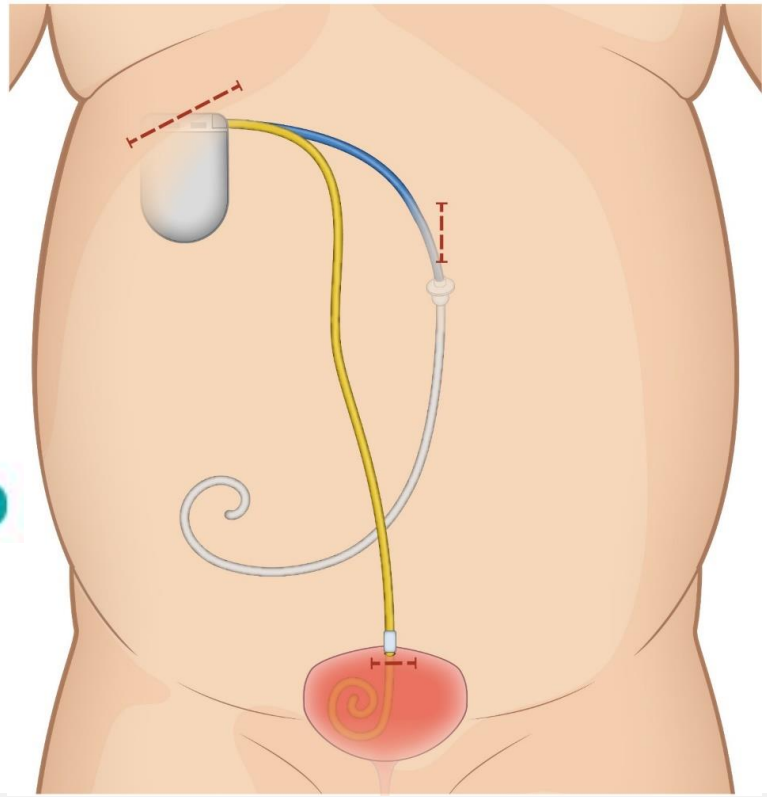
High Cost, Limited Availability

alfapump®

alfapump® strong clinical and economic rationale

Over 900 implants and hundreds of years of patient experience

DirectLink Technology



- Reduced burden of disease
- Improved patient QoL
- Cost savings for hospitals and payers

Estimated treatment cost / patient*:

LVP: ~$54K		**alfapump®: ~$35K**
~$1.8K / LVP(1)		~$25K / **alfa**pump
2 LVP / month		~$10K / implantation
15 months		

** Management estimate of US treatment costs, assuming no complications*

QoL: Quality of Life; LVP: Large Volume Paracentesis

CE

EASL The Home of Hepatology

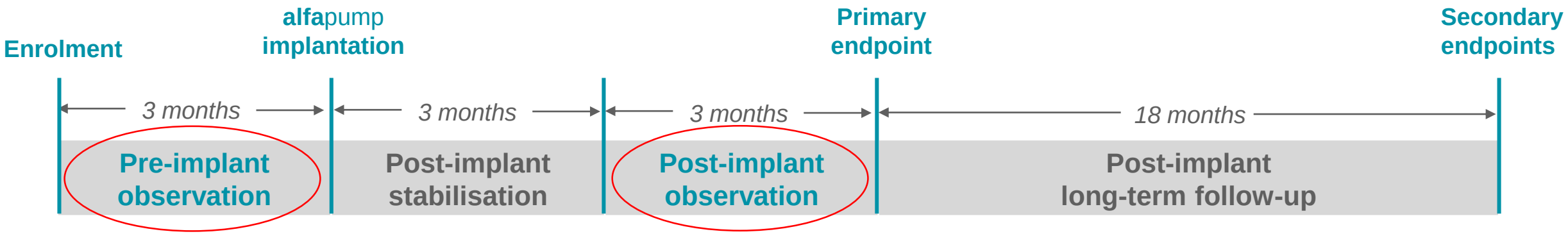
NICE National Institute for Health and Care Excellence

1913 DGVS Deutsche Gesellschaft für Gastroenterologie, Verdauungs- und Stoffwechselkrankheiten

FDA **Breakthrough Device** Designation

North American Pivotal Study (POSEIDON) underway

Pivotal Cohort of up to 50 implanted patients; Roll-In ("training") cohort of up to 40 patients



POSEIDON Study Endpoints	
Primary efficacy:	1) 50% reduction in average monthly frequency of Therapeutic Paracentesis ("TP") post-implant vs. pre-implant
	2) 50% of patients achieve a 50% reduction in the requirement for TP post-implant vs. pre-implant
Primary safety:	Rate of **alfa**pump related re-interventions adjudicated by the Clinical Events Committee (CEC)
Secondary:	QoL (SF36, Ascites-Q), nutritional status, health economics, safety (device and/or procedure-related AEs), survival

***QoL**: Quality of Life; **AE:** Adverse Event*

Interim POSEIDON: Positive for primary endpoints

Data from 26 Roll-In patients

EFFICACY

- ✓ Over 90% reduction in mean Therapeutic Paracentesis (TP) frequency (primary endpoint >50% reduction)
- ✓ 100% patients with > 50% reduction in mean TP frequency per month (primary endpoint >50% of patients)

SAFETY

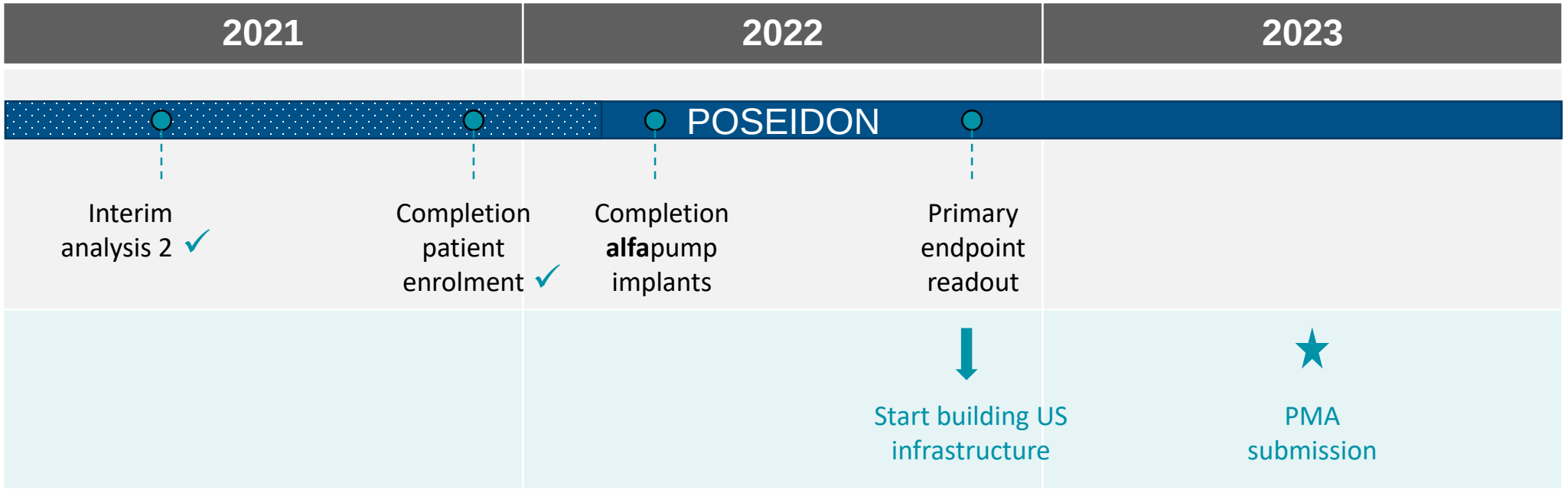
- ✓ In line with expectations – 3 composite primary safety events

QUALITY OF LIFE

- ✓ Clinically important improvement maintained for up to 12 months post-implantation

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

Pursuing North American alfapump® approval



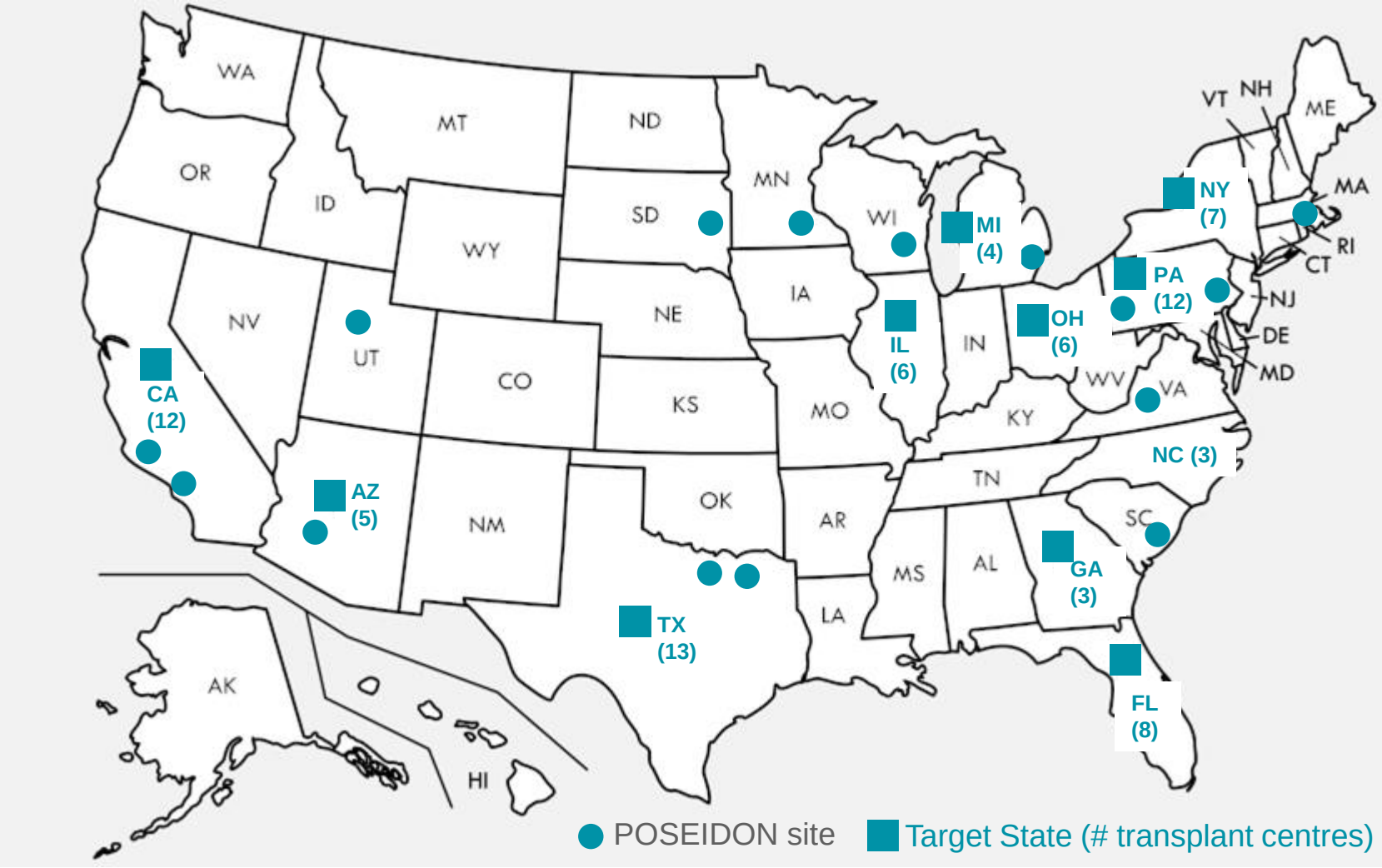
NTAP for breakthrough devices de-risks reimbursement in key Medicare population

CMS
CENTERS FOR MEDICARE & MEDICAID SERVICES

PMA: *Pre-Market Approval;* ***NTAP:*** *New Technology Add-On Payment*

Note: Presented timelines are subject to further developments related to the COVID-19 pandemic

US commercialisation through our specialty salesforce



Initial focus on key transplant centres

~50-person team:

35 sales reps, 10 clinical, 5 corporate

DSR®

Breakthrough approach to **persistent congestion in heart failure** leveraging proven **alfa**pump® platform

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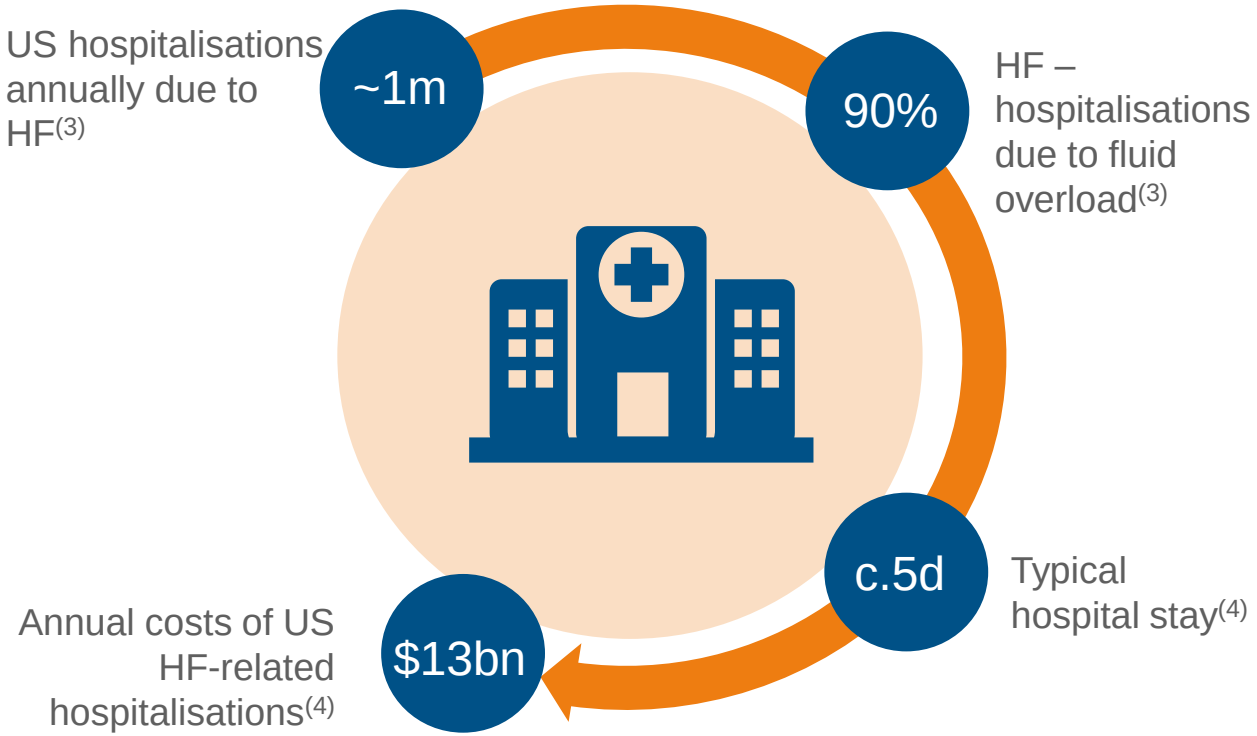
Diuretic-resistant congestion in heart failure

Clear unmet clinical need and driver of costs for heart failure patients



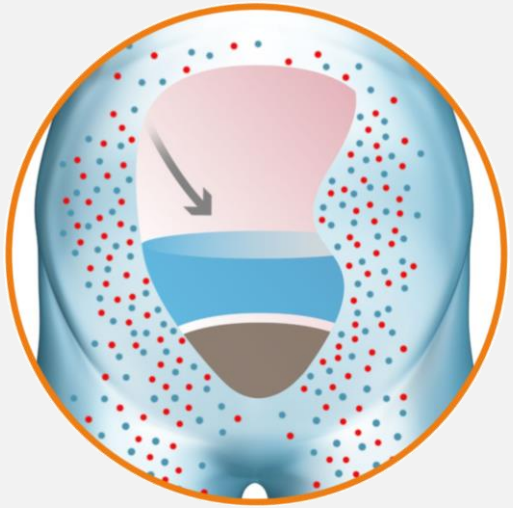
- *40% of heart failure patients on IV loop diuretics have a poor response(1)*
- *24% re-admission rate at 30 days(2)*

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: Kilgore et al. (2017)

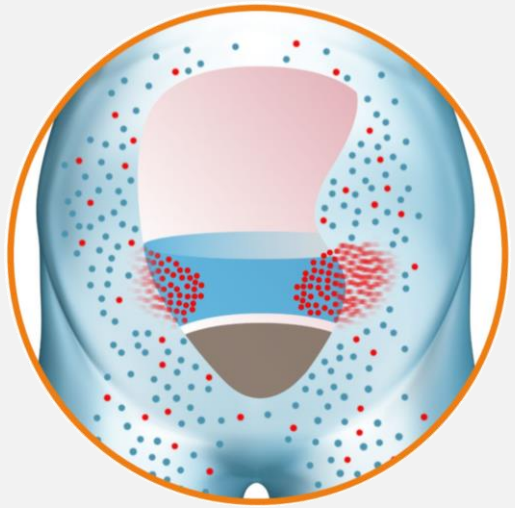
Direct Sodium Removal (DSR®) platform

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

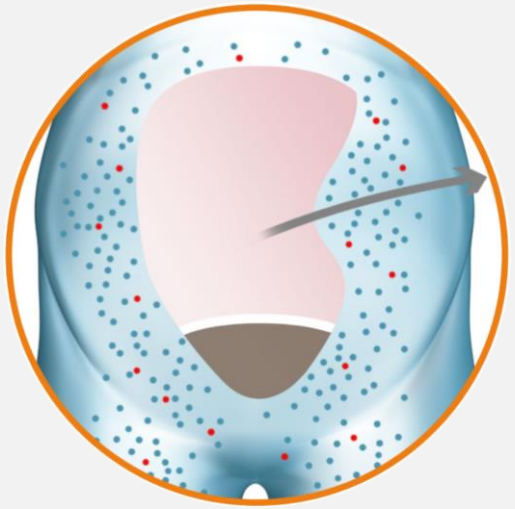
1. **Sodium-free DSR infusate administered to peritoneal cavity**



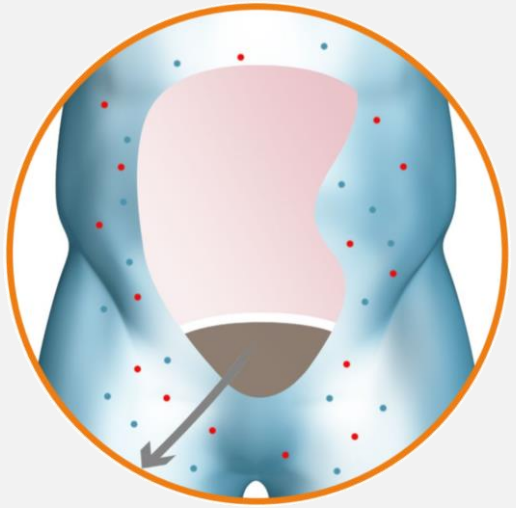
2. **Sodium diffuses from body into DSR infusate**



3. **DSR infusate + extracted sodium removed from the body**



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

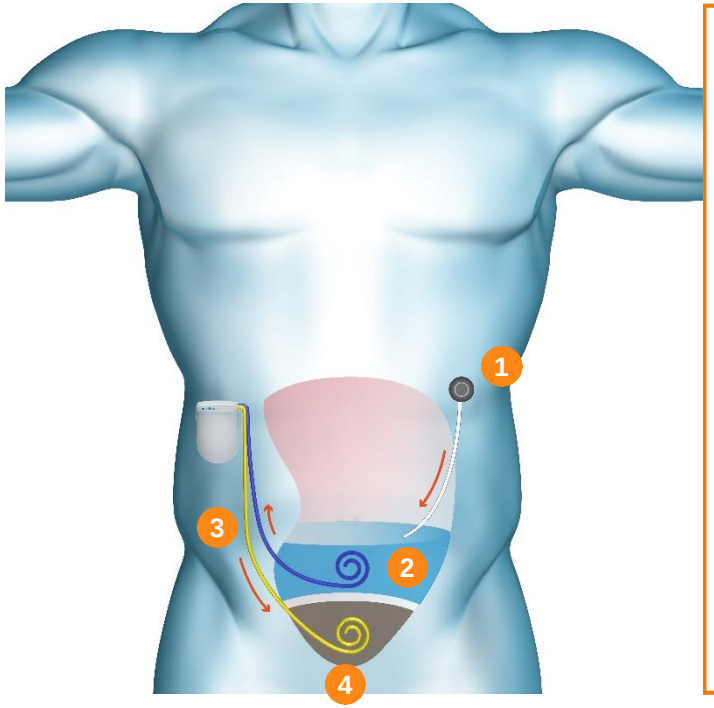


- water
- sodium

Fundamental patents to reduce fluid overload in heart failure patients granted in the US and Europe

alfapump DSR® leveraging proven alfapump® platform

Fully implanted system for long-term DSR® therapy – keeping patients out of the hospital



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

RED DESERT: Successful Proof-of-Concept Study

8 euvolemic heart failure 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

Presented as Late-Breaker and Highlight at Heart Failure 2021

Significant improvement in cardio-renal function

- 30% decrease* in NT-proBNP** ($p<0.001$)
- 22% increase* in eGFR** ($p<0.001$) / 22% decrease* in creatinine** ($p<0.001$)

Dramatic and sustained improvement in diuretic response

- End of 6-week study: over 150% increase** in diuretic response***
- Long-term follow-up (9-19 months after study completion): 40-96% reduction in diuretic dose at last visit during follow-up

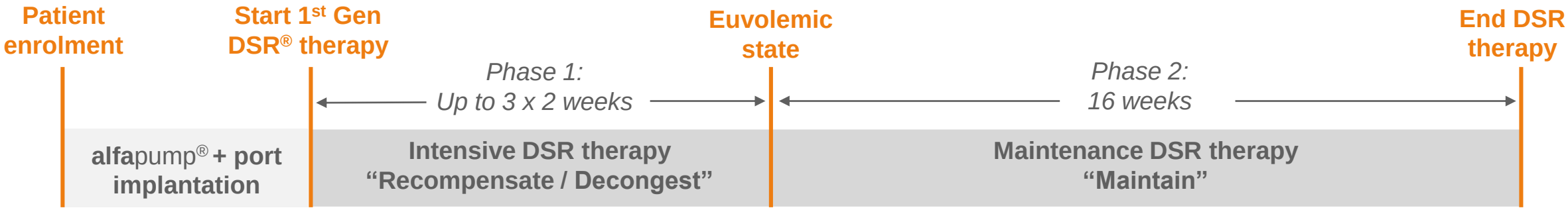
"Simultaneous normalisation of diuretic response and improvement in cardio-renal status is a never before seen treatment effect" – Dr. Testani, Yale

** 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 DESERT: Ph. 2A in target patient population

20 decompensated heart failure patients with persistent congestion on high dose diuretics – ongoing



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
- **Exploratory:** evaluate potential impact of SGLT-2 inhibitors on DSR therapy*

** patients will be randomised 1:1 to DSR therapy +/- SGLT-2 inhibitor therapy*

SAHARA DESERT: Ph. 2A positive interim data

Indication of strong safety and efficacy in 6 patients

Safe, effective and rapid elimination of persistent congestion and restoration of euvolemia without any loop diuretics

- Mean weight loss of ~6kg (=7% of body weight) vs. baseline

Considerable benefit in cardio-renal status

- Reduction* in NT-proBNP >30% vs. baseline
- eGFR* and creatinine* similar to baseline
  - Worsening in kidney function is normally expected during significant volume removal

Dramatic improvement in diuretic responsiveness for months post-treatment

- End of phase 1 (n=6***): more than doubling* of sodium excretion** (near normal levels)
- 3 months* after end of Phase 1 (n=4): less than 10% of their baseline loop diuretic dose

"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

mean value; ** assessed by 6-hour excretion of sodium after IV administration of 40mg furosemide * one patient has completed first 2-week dosing in phase 1 and is about to enter second 2-week dosing in phase 1*
***NT-proBNP**: N-terminal-pro hormone B-type Natriuretic Peptide (analysed in local lab); **eGFR**: estimated glomerular filtration rate*

Proprietary heart failure drug development programme

Red Desert PoC ✓
- 1st Gen. Infusate + **alfa**pump
- 8 stable HF patients
- Pos. outcome

Sahara Desert Ph. 2A ongoing
- 1st Gen. Infusate + **alfa**pump
- Up to 20 decompensated HF patients
- Pos. interim data

2nd Gen. Infusate Development
- Animal GLP and CMC data in H2 '22

Mojave Desert Ph. 1B/2A (US)
- 2nd Gen. Infusate (no **alfa**pump)
- Decompensated HF patients

Sonoran Desert Ph. 2A (US)
- 2nd Gen. Infusate + **alfa**pump
- Decompensated HF patients

1st Generation Infusate

- ✓ Sodium-free D10% (off-the-shelf)
- ✓ Clinical Proof-of-Concept
- ✓ Rapid clinical path

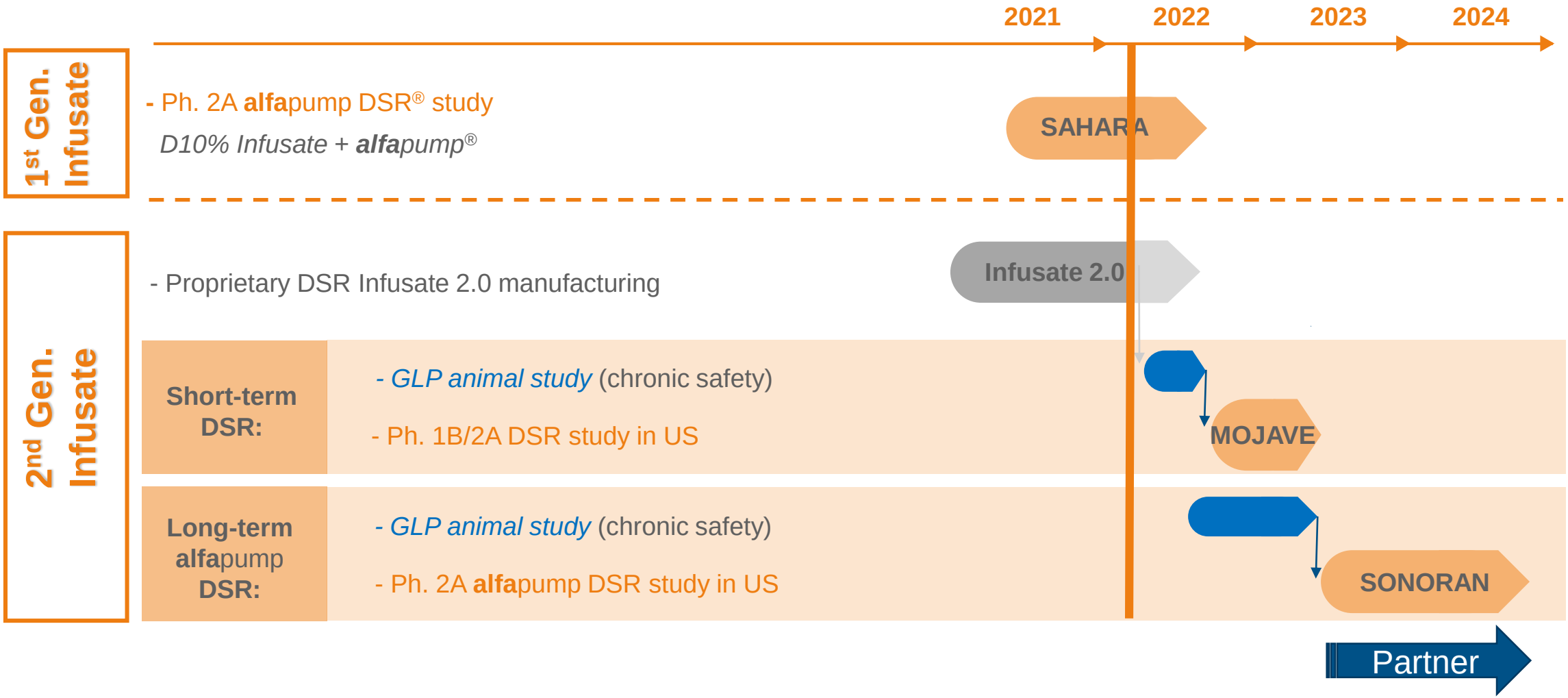
2nd Generation Infusate

- ✓ Sodium-free dextrose / icodextrin (proprietary)
- ✓ Improved therapeutic profile
- ✓ Favorable safety profile
- ✓ IP protection drives recurring revenue from high gross margin consumable

PoC: *Proof-of-Concept;* ***HF:*** *Heart Failure;* ***GLP:*** *Good Laboratory Practices;* ***CMC:*** *Chemistry, Manufacturing & Controls*

DSR® – plan to partner after US efficacy study

Step-by-step approach to introduction of breakthrough therapy in decompensated HF patients



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

Outlook

Strong **near term value drivers**

with clear **long term potential**

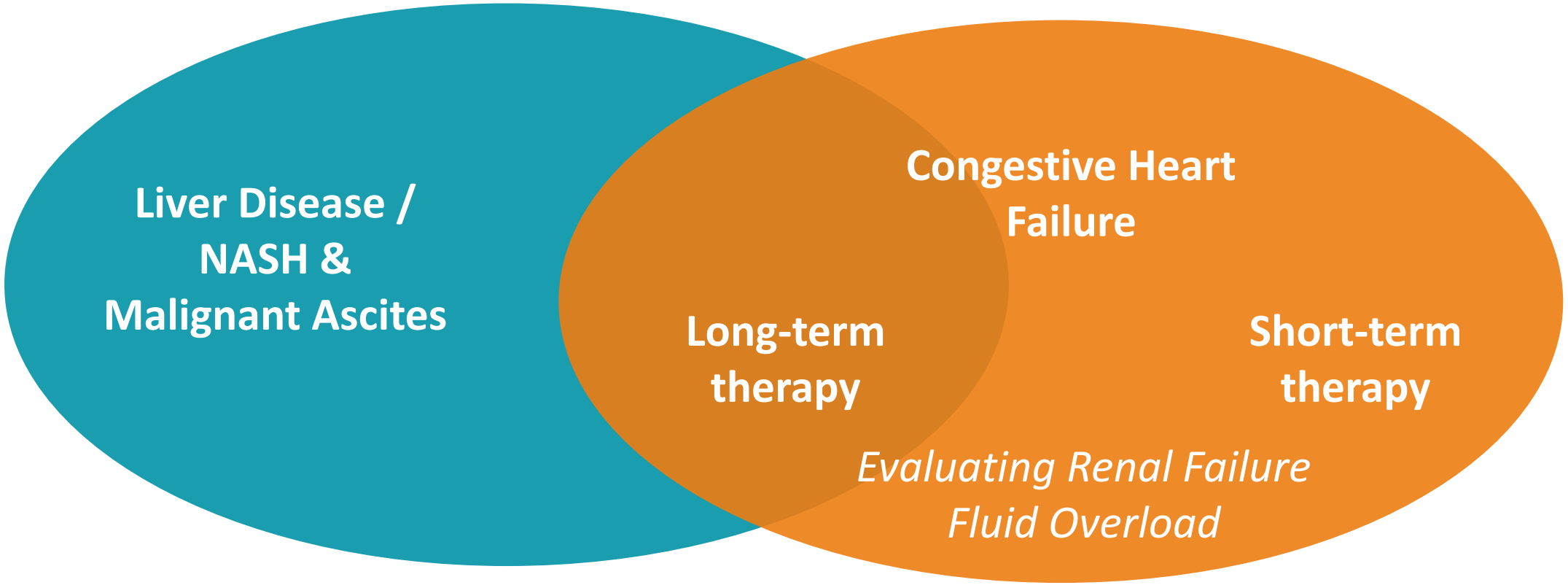
Building on our two proprietary platforms

Complementary approaches to diuretic-resistant fluid overload

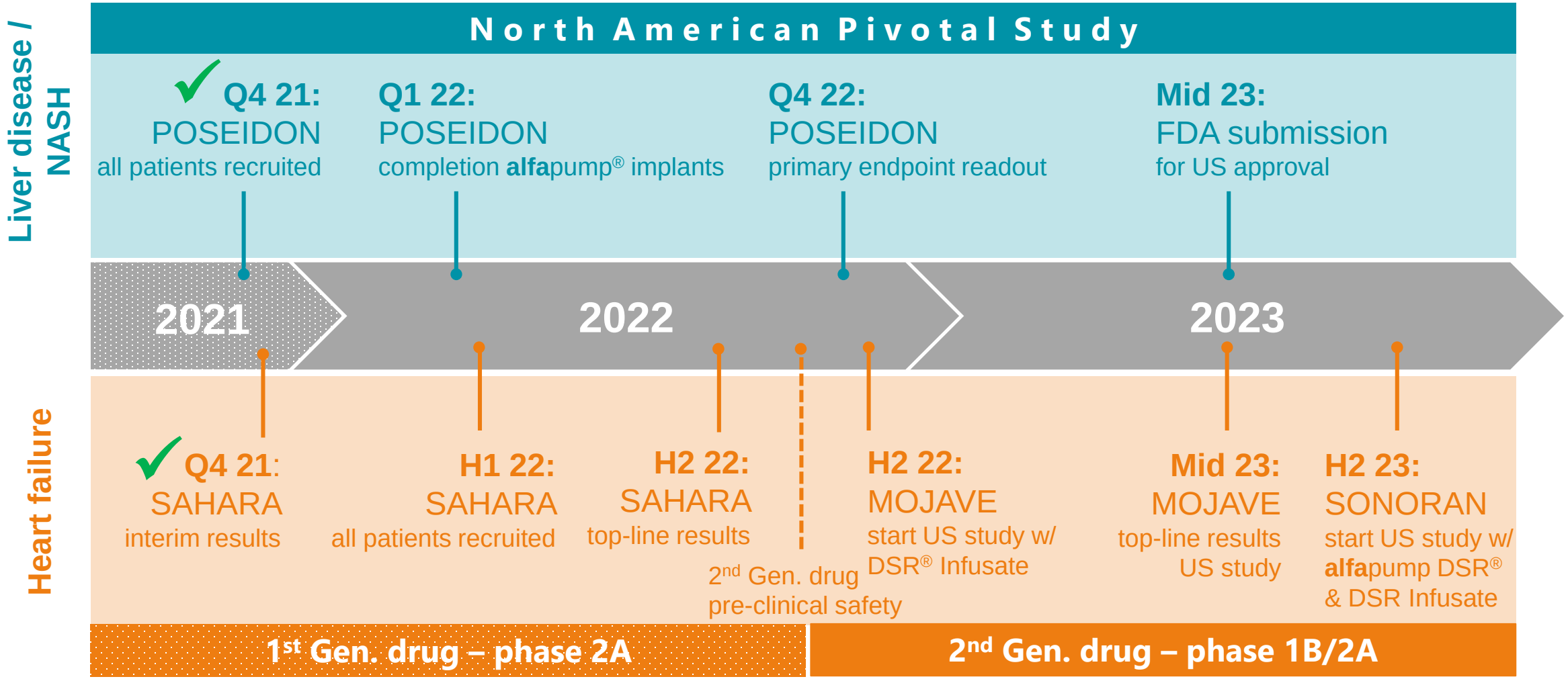
alfapump®

alfapump DSR®

DSR®



Strong outlook for value drivers



Note: Presented timelines are subject to further developments related to the COVID-19 pandemic

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