

**sequana**medical

Euronext: SEQUA.BR

BTIG virtual Conference – 16 February 2022

Ian Crosbie, CEO

## Innovators in the treatment of diuretic-resistant fluid overload

liver disease  malignant ascites  heart failure

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- The **alfapump**<sup>®</sup> system has not yet received regulatory approval in the United States and Canada. Any statement in this presentation about safety and efficacy of the **alfapump**<sup>®</sup> system does not apply to the United States and Canada. In the United States and Canada, the **alfapump**<sup>®</sup> 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](http://www.poseidonstudy.com).
- DSR<sup>®</sup> 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<sup>®</sup> therapy is currently not approved for clinical research in the United States or Canada. There is no link between DSR<sup>®</sup> therapy and ongoing investigations with the **alfapump**<sup>®</sup> 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:

- alfapump**<sup>®</sup> is a registered trademark. DSR<sup>®</sup> and **alfapump DSR**<sup>®</sup> are registered trademarks in the Benelux, China, the EU, United Kingdom, and Hong Kong.

# Uniquely positioned in two large markets



- **alfapump<sup>®</sup> in liver disease – over €3 Bn / year <sup>(1)</sup>**
  - 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

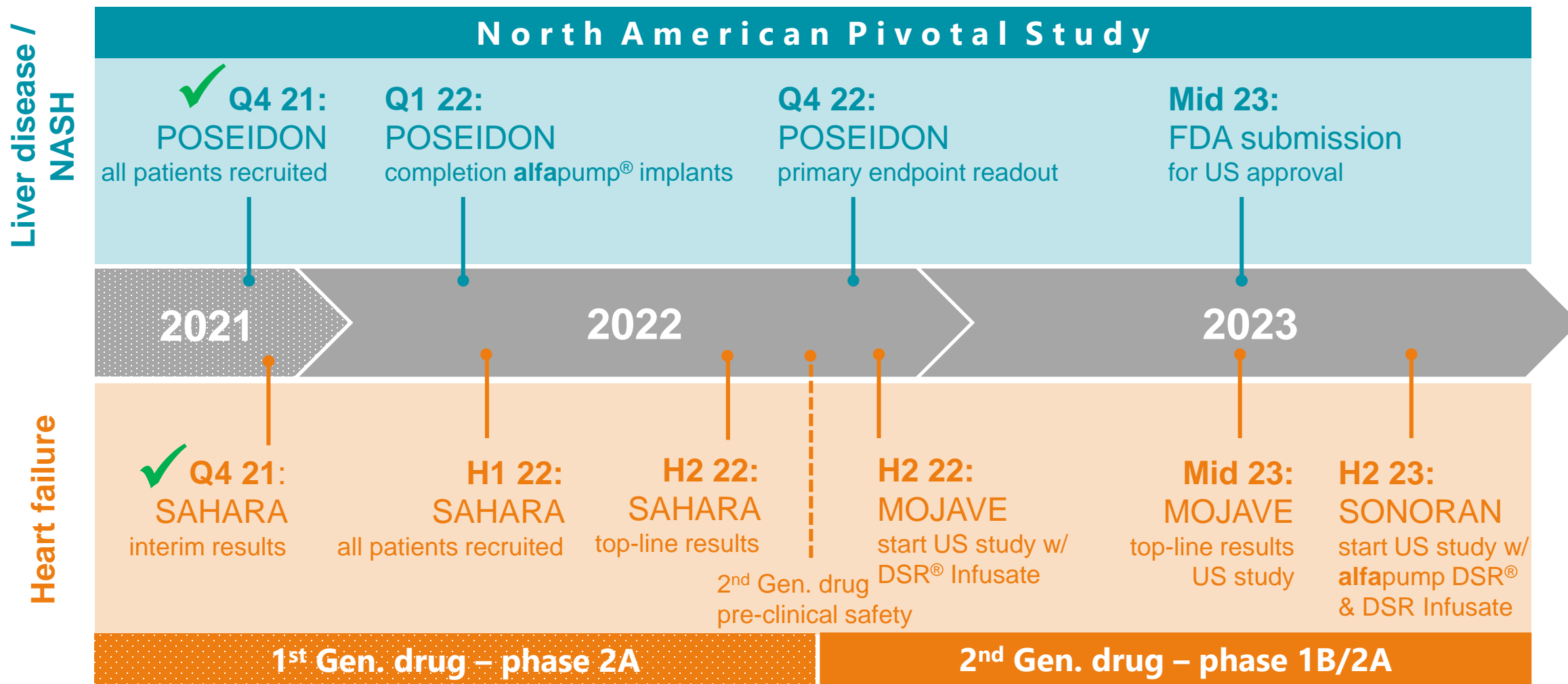


- **DSR<sup>®</sup> in heart failure – over €5 Bn / year <sup>(2)</sup>**
  - Clinical proof-of-concept established
  - Ph. 2A 1<sup>st</sup> Gen. drug – positive interim data
  - Low-risk proprietary 2<sup>nd</sup> Gen. drug – in development
  - Partnering after US efficacy study



- **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**

# Strong outlook for value drivers



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








**alfapump<sup>®</sup>**

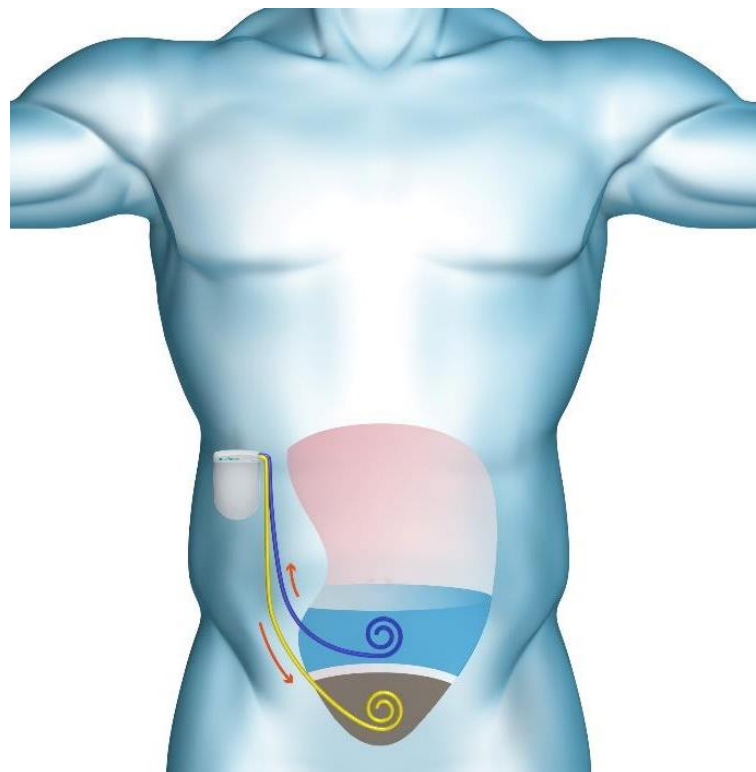
Proven step change in the  
treatment of liver refractory  
ascites






# 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

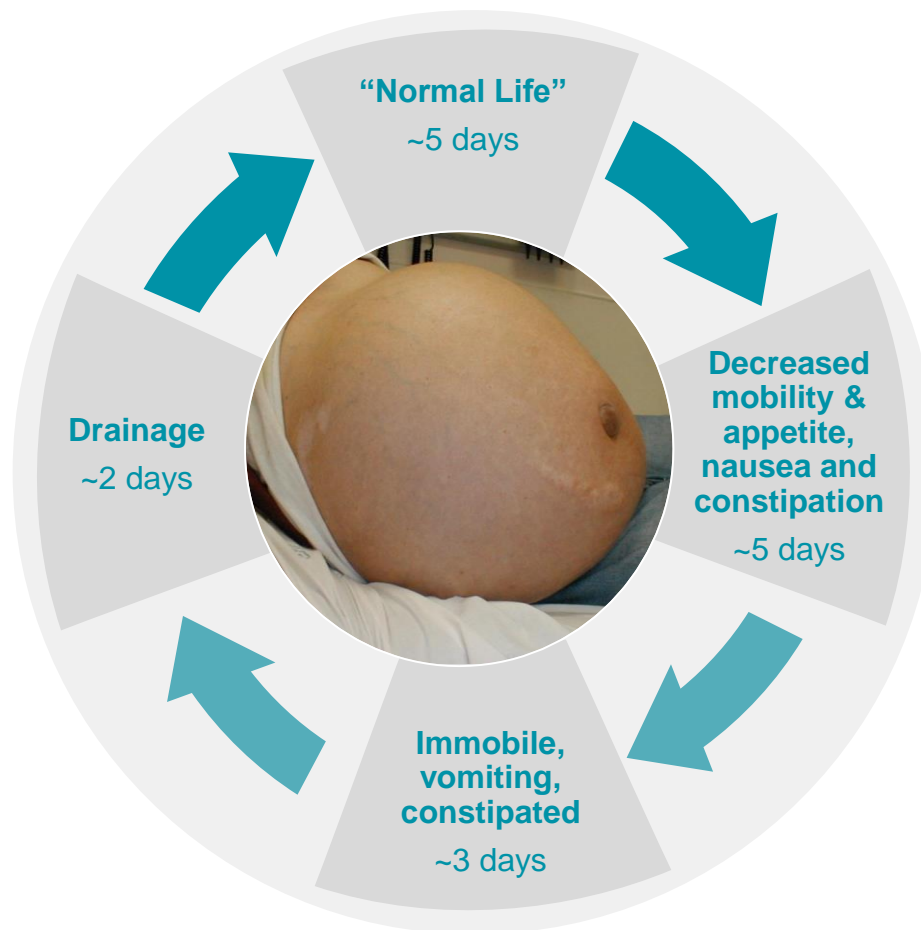


-  Easy implantation
-  Long-term implantation & catheter patency
-  Moves up to 4 litres / day
-  Virtually non-clogging
-  No significant heating during charging and operation

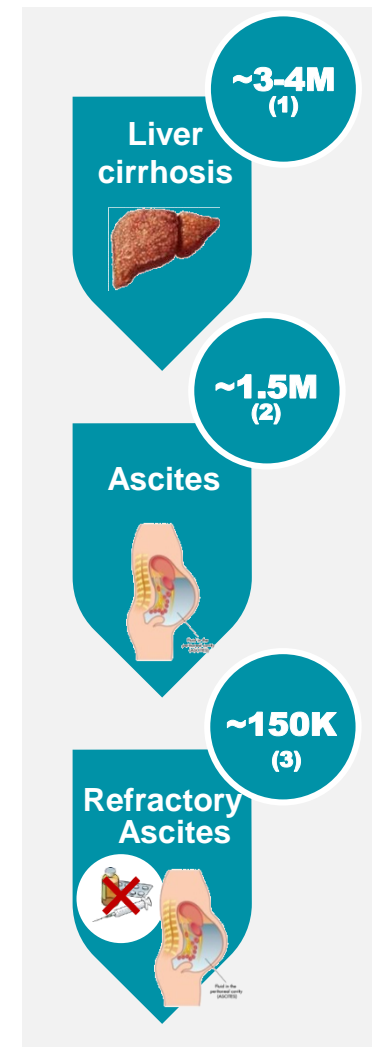
***Proven capabilities – over 900 systems implanted***  
***Strong IP barriers through extensive patent portfolio & know-how***

# Refractory ascites – key complication of liver cirrhosis

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



Typical patient life<sup>(4)</sup>



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; Nouredin 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





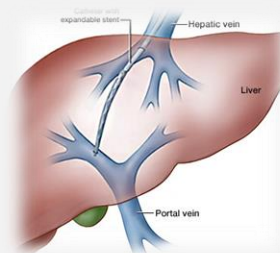
# Limitations of existing therapies

## 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



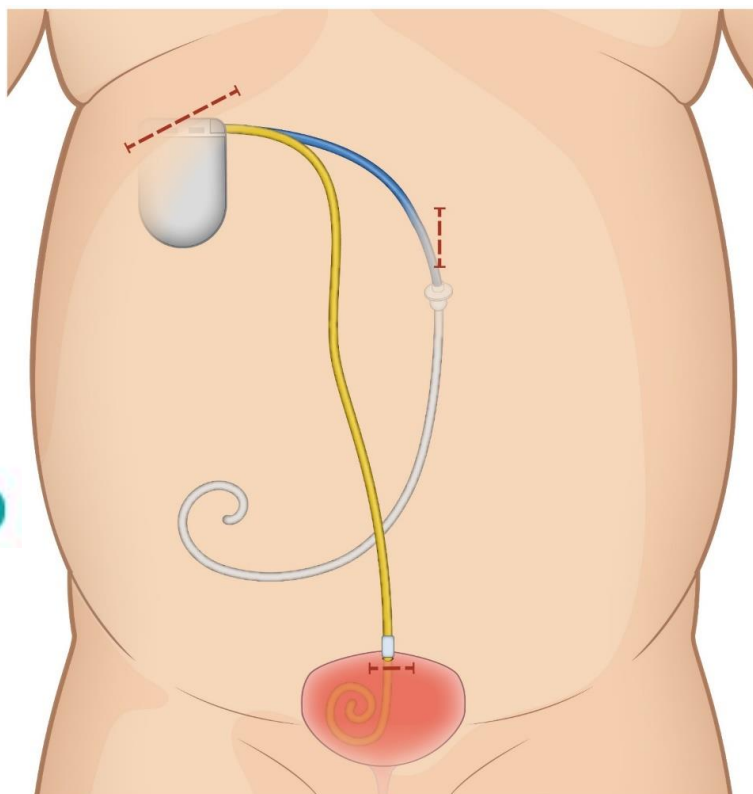
High Cost, Limited Availability

**alfapump®**



# alfapump® strong clinical and economic rationale

Over 900 implants and hundreds of years of patient experience



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

Estimated treatment cost / patient\*:

**LVP: ~\$54K** ↔ **alfapump®: ~\$35K**

~\$1.8K / LVP<sup>(1)</sup>      ~\$25K / alfapump  
 2 LVP / month      ~\$10K / implantation  
 15 months

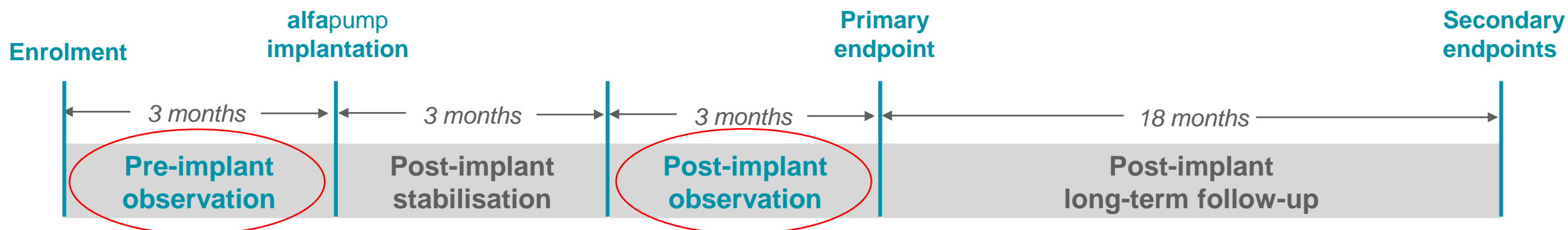
\* Management estimate of US treatment costs, assuming no complications

QoL: Quality of Life; LVP: Large Volume Paracentesis



# 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 **alfapump** 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

# 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)

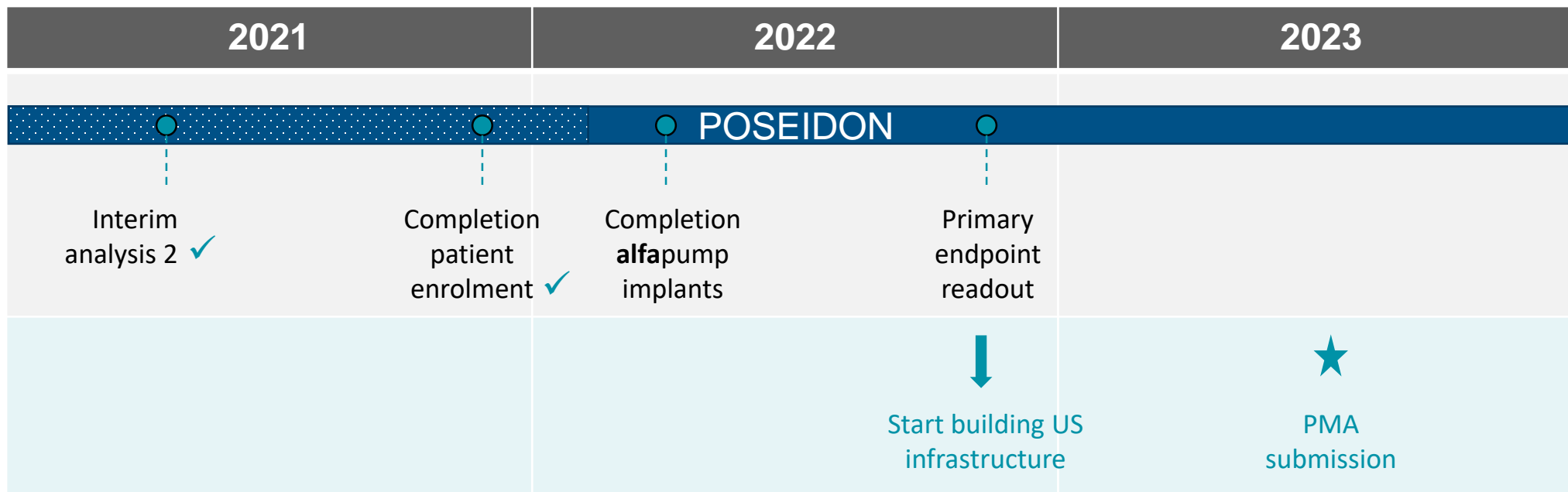
## SAFETY

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

## QUALITY OF LIFE

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

# Pursuing North American alfapump<sup>®</sup> approval



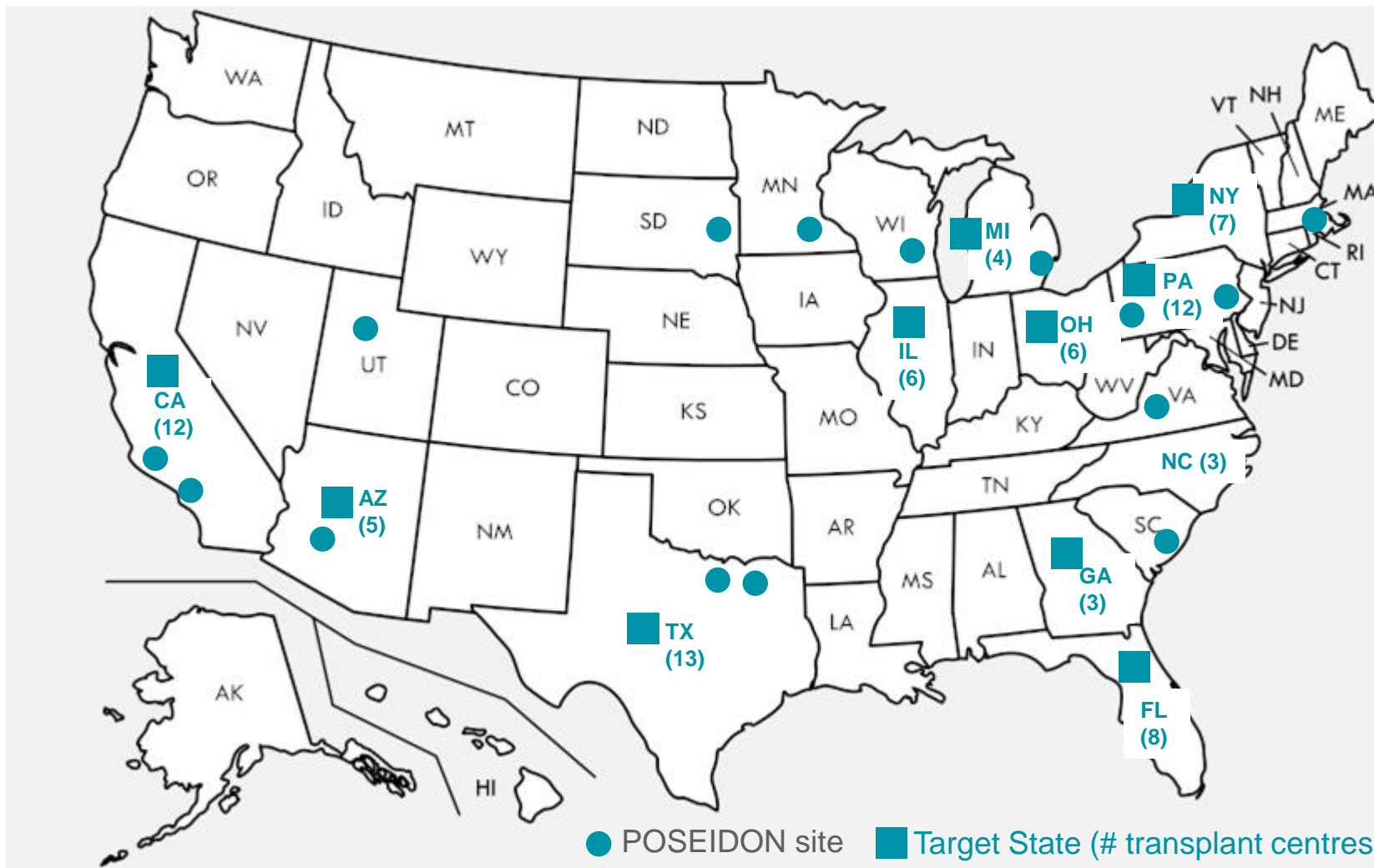
*NTAP for breakthrough devices de-risks reimbursement in key Medicare population*



*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

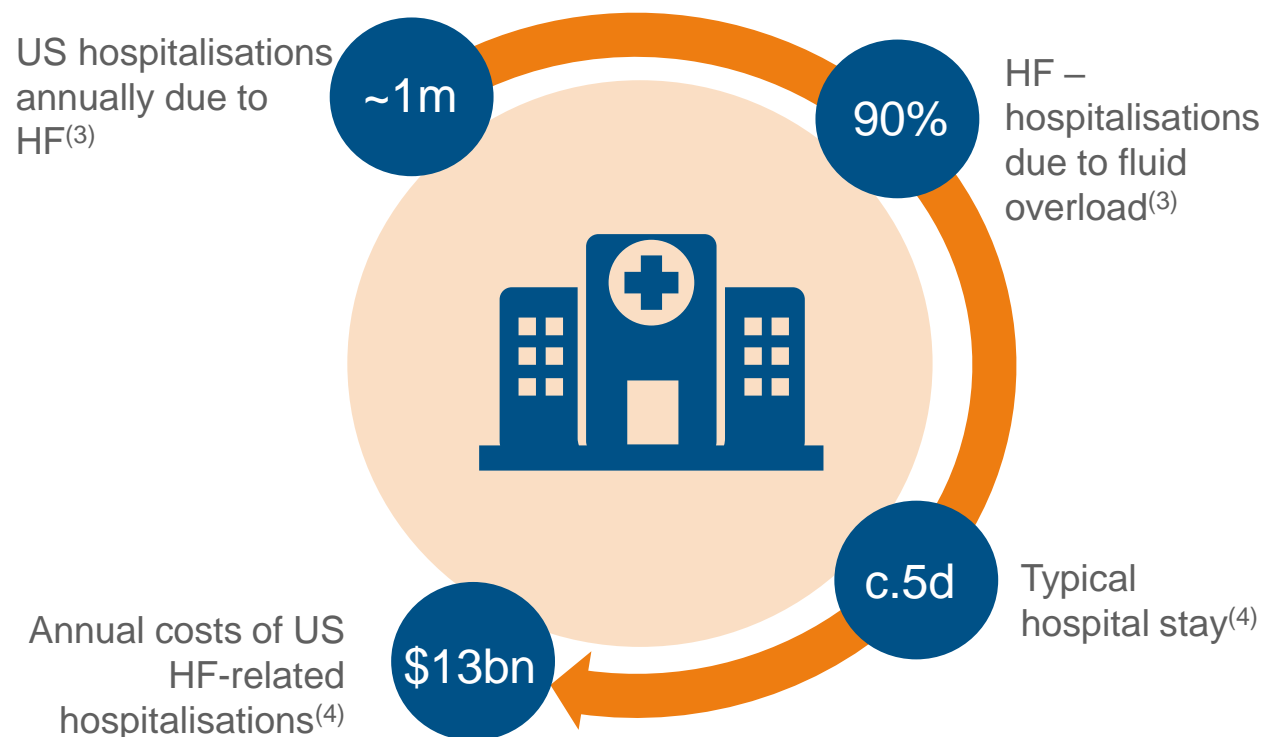
An elderly couple is walking hand-in-hand in a park. The man on the left is wearing a maroon sweater over a blue collared shirt and light-colored pants. The woman on the right is wearing a blue cardigan over a black and white polka-dot top and jeans. They are both smiling and looking towards the right. The background is a bright, sunny outdoor setting with green trees and a clear sky.

**DSR<sup>®</sup>**

Breakthrough approach to  
**persistent congestion in heart  
failure** leveraging proven  
**alfapump<sup>®</sup>** platform

# 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<sup>(1)</sup>*
- *24% re-admission rate at 30 days<sup>(2)</sup>*



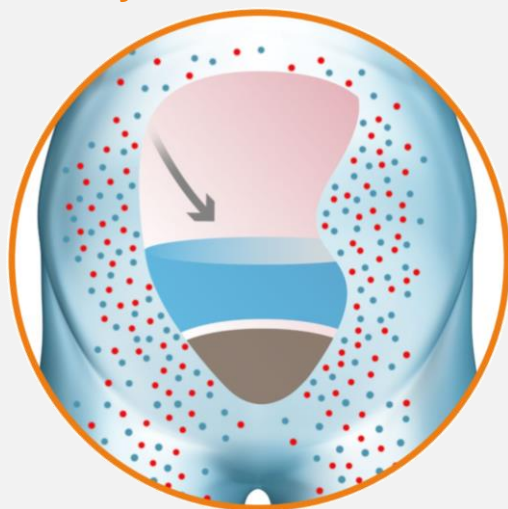


# Direct Sodium Removal (DSR<sup>®</sup>) platform

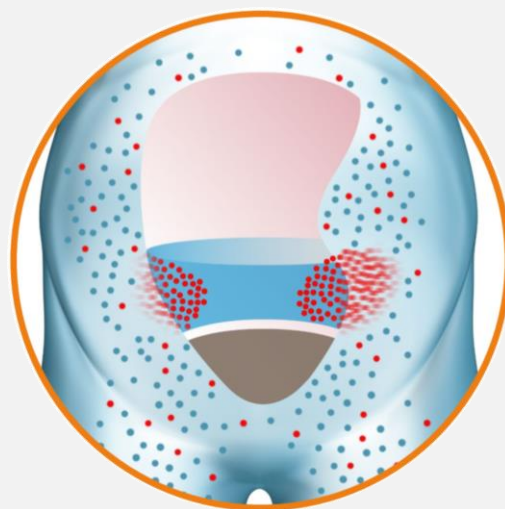
Eliminating fluid spread across the body – working in partnership with the kidneys



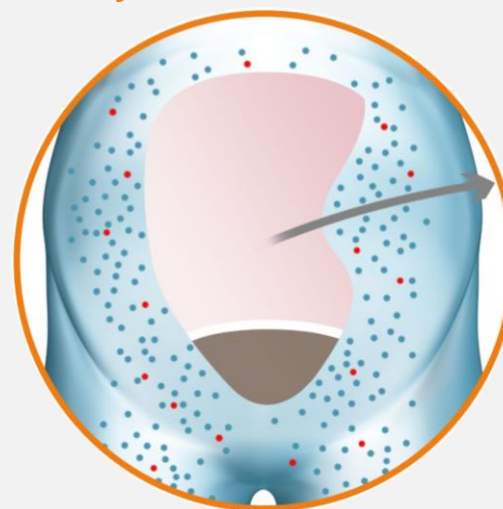
**1** Sodium-free DSR infusate administered to peritoneal cavity



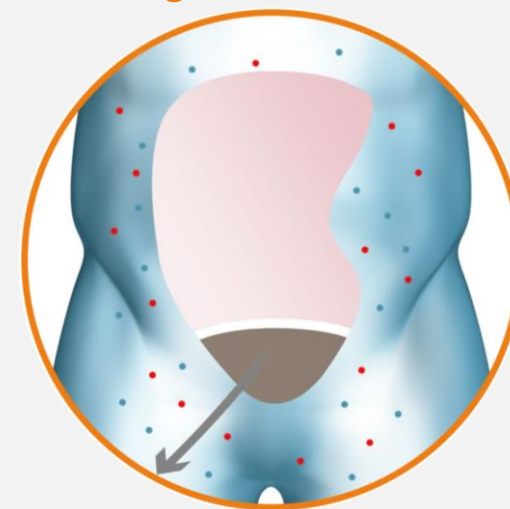
**2** Sodium diffuses from body into DSR infusate



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



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

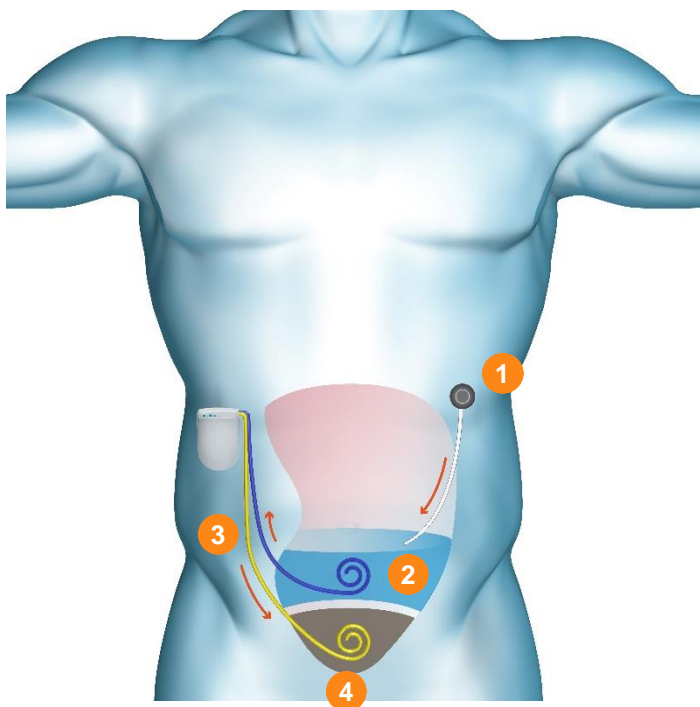


- water
- sodium

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

# alfapump DSR<sup>®</sup> leveraging proven alfapump<sup>®</sup> platform

Fully implanted system for long-term DSR<sup>®</sup> 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 **alfapump** 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

## 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

Presented as  
Late-Breaker and  
Highlight at  
Heart Failure 2021

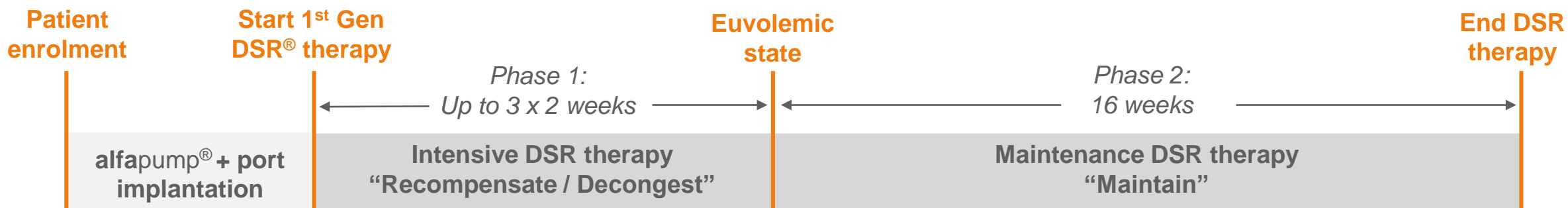
***“Simultaneous normalisation of diuretic response and improvement in cardio-renal status is a never before seen treatment effect” – Dr. Testani, Yale***

\* 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 **alfapump** 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**

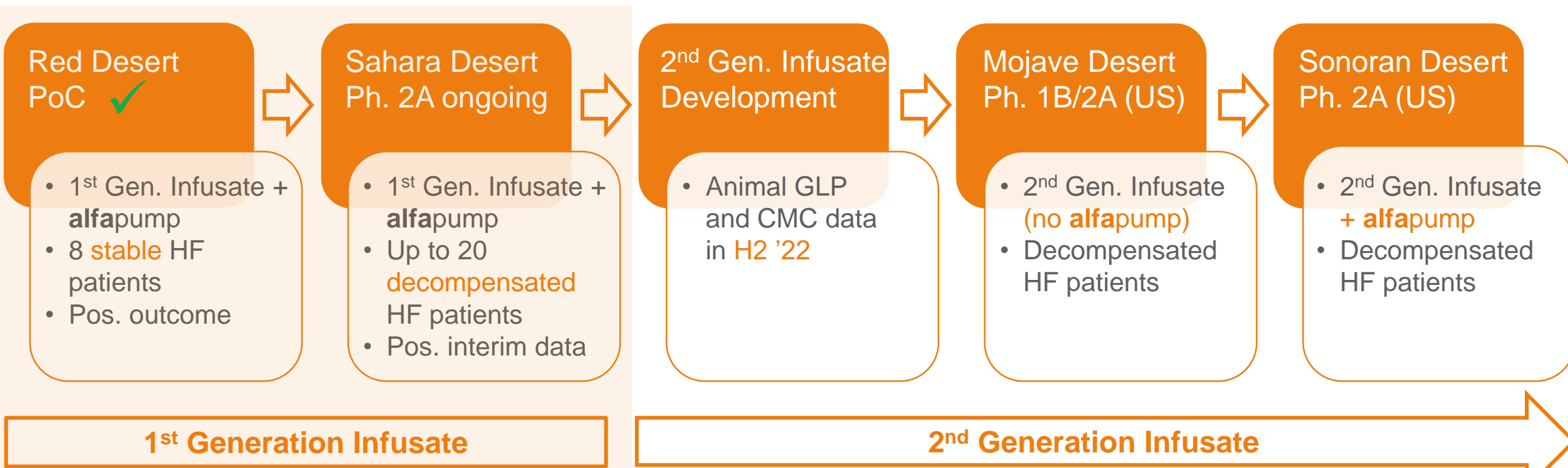
- Reduction\* in NT-proBNP >30% vs. baseline
- eGFR\* and creatinine\* similar to baseline
  - Worsening in kidney function is normally expected during significant volume removal

**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***

# Proprietary heart failure drug development programme

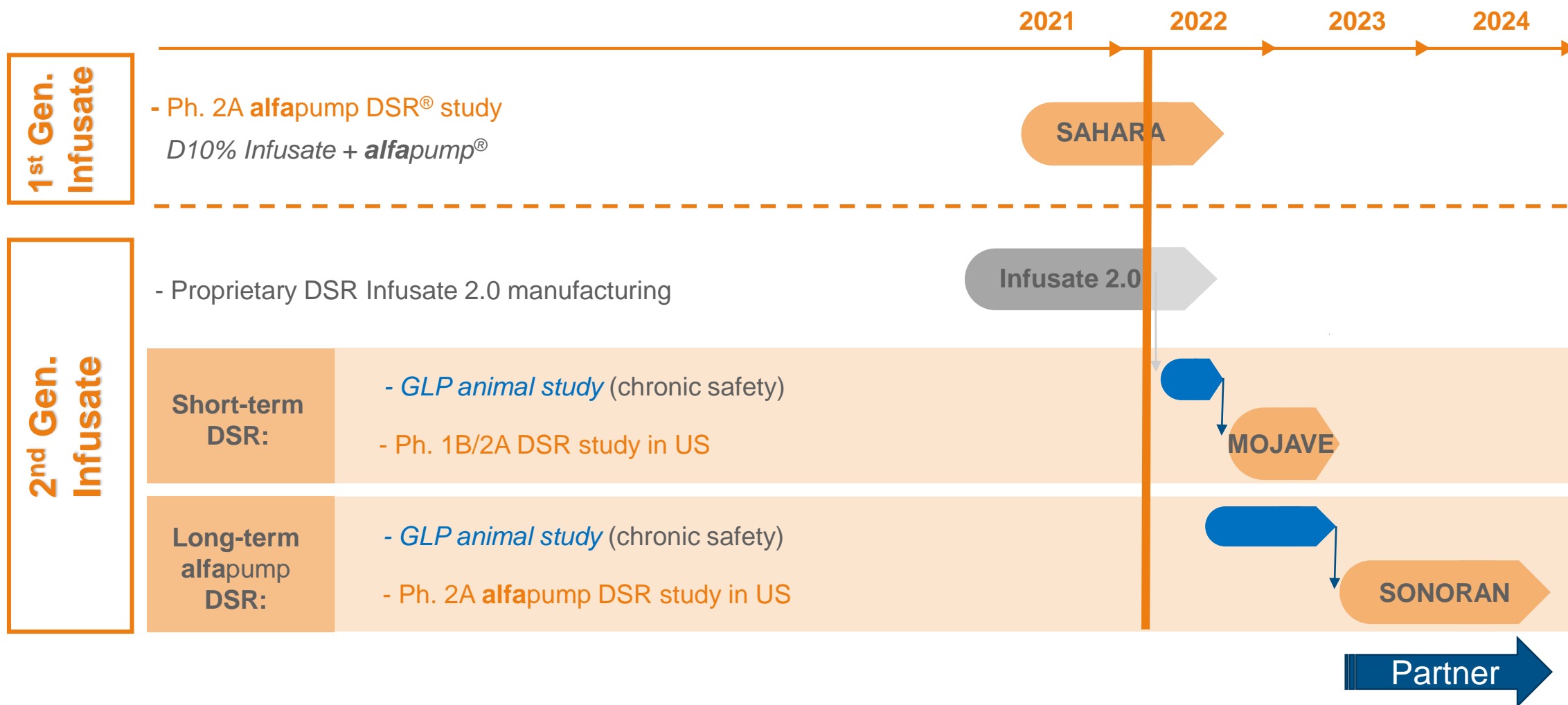


- ✓ Sodium-free D10% (off-the-shelf)
- ✓ Clinical Proof-of-Concept
- ✓ Rapid clinical path

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

# DSR<sup>®</sup> – 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**





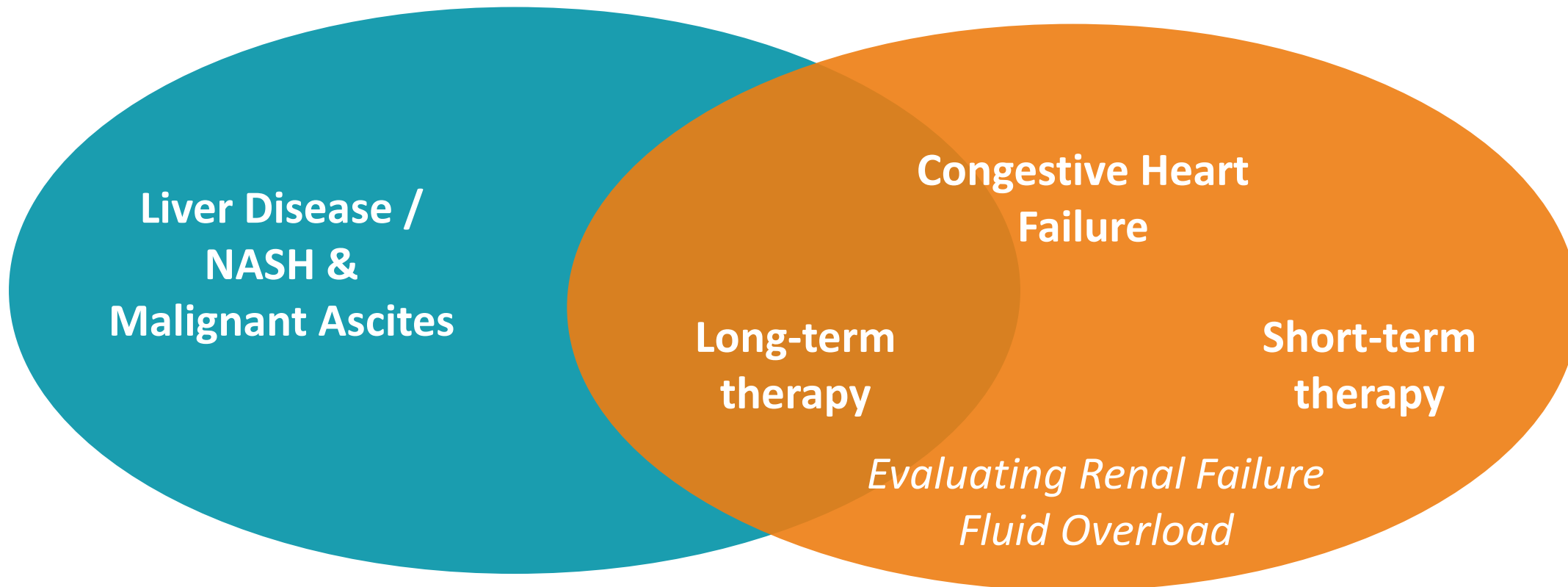
# Building on our two proprietary platforms

Complementary approaches to diuretic-resistant fluid overload

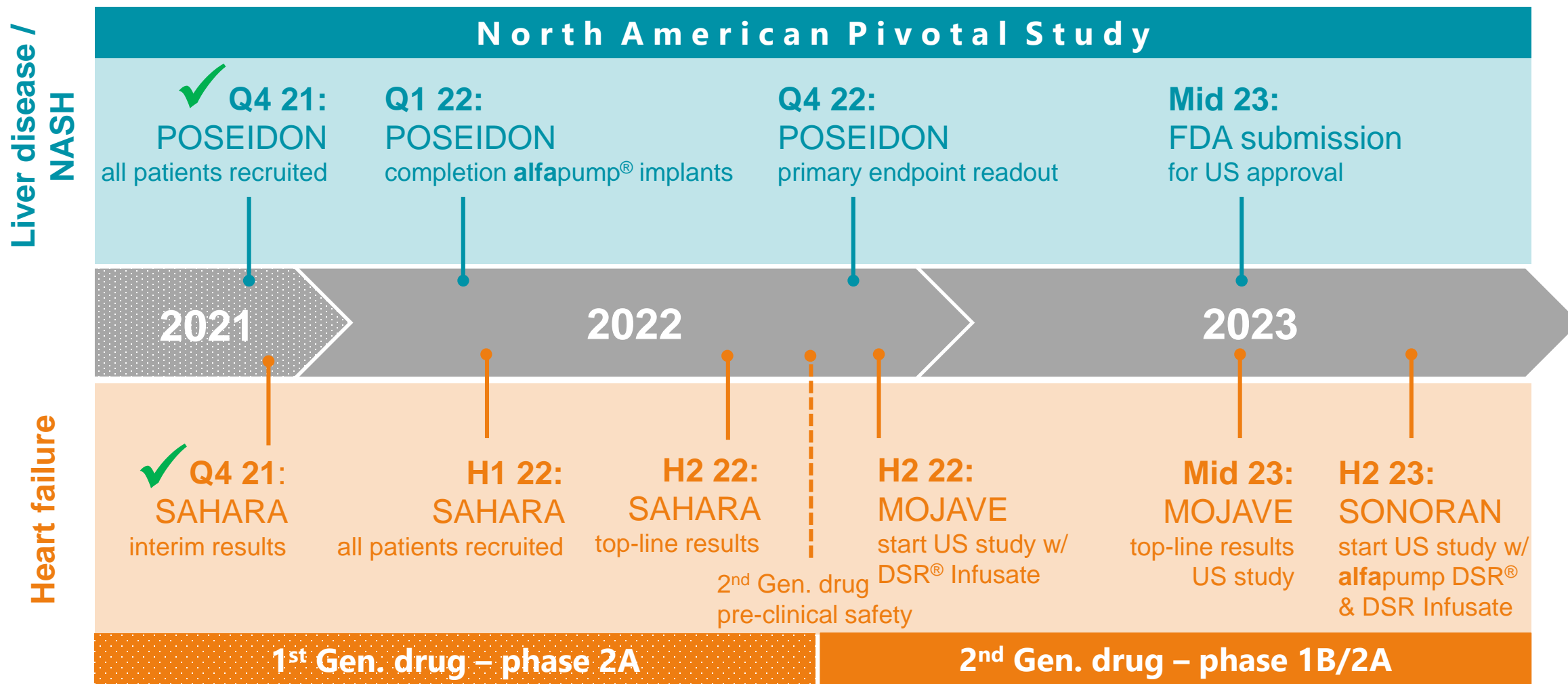
alfapump® 

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# Strong outlook for value drivers



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

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