XVIVO

XVIVO Capital Markets Day

September 23, 2021

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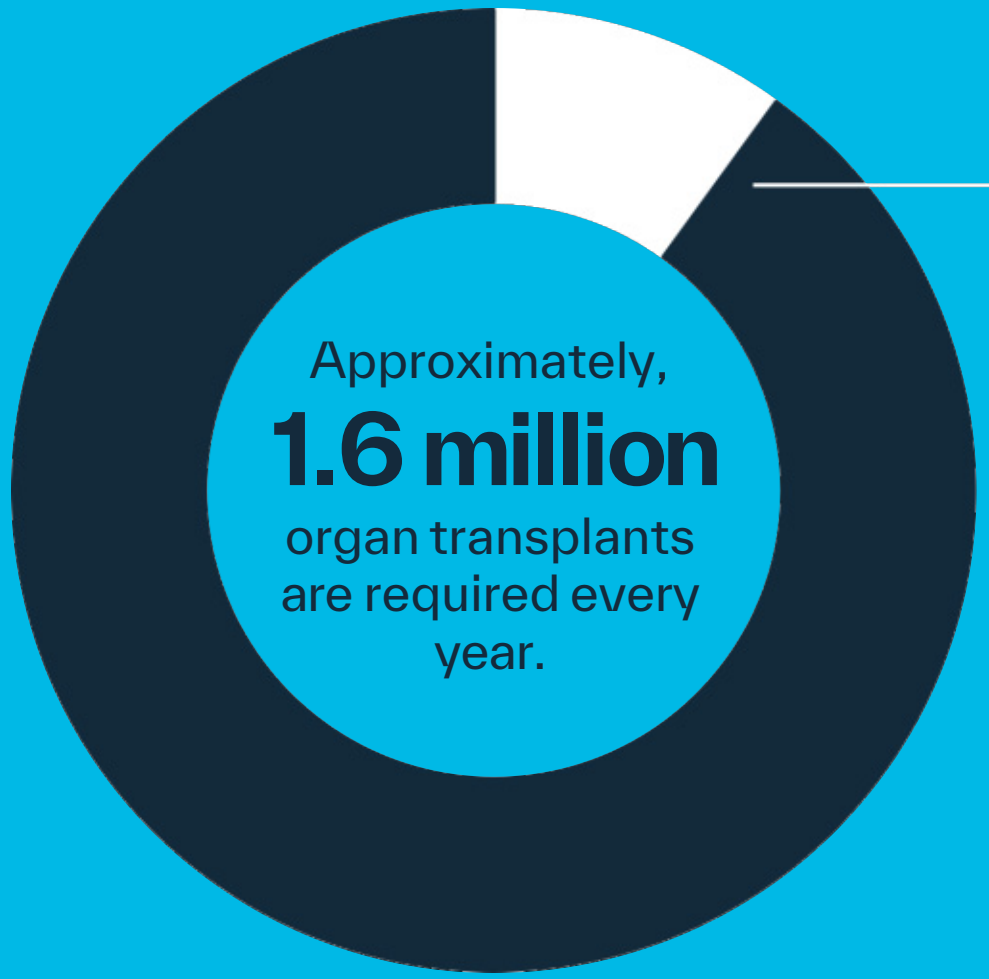
Agenda

13.00	- 13.05	Introduction	Lars Frick, Moderator and Dag Andersson, CEO
13.05	- 13.20	Market & trends	Dag Andersson, CEO
13.20	- 13.35	Strategy	Dag Andersson, CEO and Kristoffer Nordström, CFO
13.35	- 13.50	Health economics	Johan Holmström, CCO
13.50	14.05	Q&A	
14.05	- 14.20	Break	
14.20	- 14.50	Heart	Andreas Wallinder, CMO and Professor Filip Rega, Cardiac surgeon at UZ Leuven
14.50	- 15.20	Abdominal	Arjan v.d. Plaats, R&D Director and Johan Holmström, CCO
15.20	15.35	Q&A	
15.35	- 15.50	Break	
15.50	- 16.20	Lung	Rodney Jones, Sales Director North America and Brandi Zofkie, Director at Lung BioEngineering
16.20	- 16.40	Future of transplantation	Christoffer Rosenblad, COO and Professor Muhammad M. Mohiuddin, Director Cardiac Xenotransplantation Program at University of Maryland
16.40	- 16.55	Q&A	
16.55	- 17.00	Thank you	Dag Andersson, CEO

The need



With only

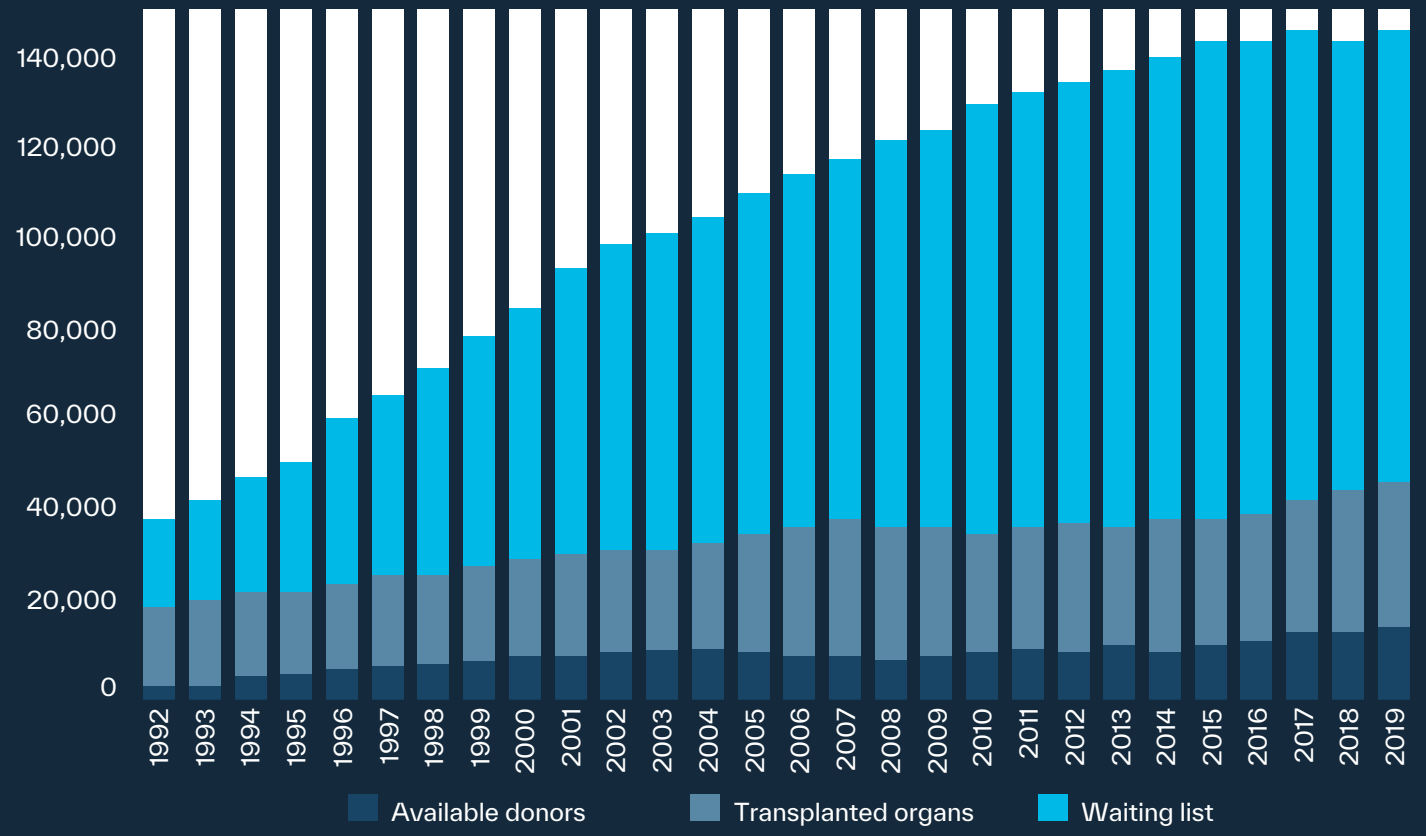
160,000

organ transplants performed globally each year, this only covers

10% of the total need.

Waiting lists

The trend (a US example)



It is estimated that approximately

150,000 patients

in the United States are currently **waiting for a new organ.**

Approximately **25% of patients** waiting for new lungs or heart **die while waiting for a new organ.**

XVIVO

Beatrice Halby,
Lung recipient

We believe in an extended life of organs

Nobody should die waiting for a new organ

Key facts

XVIVO is the first global ‘all organ’ company

Experts in advanced solutions and machines for transplantation

World leading in lung and liver transplantation

Founded in

1998

HQ in Gothenburg

Sweden

Midcap NASDAQ

Listed 2016

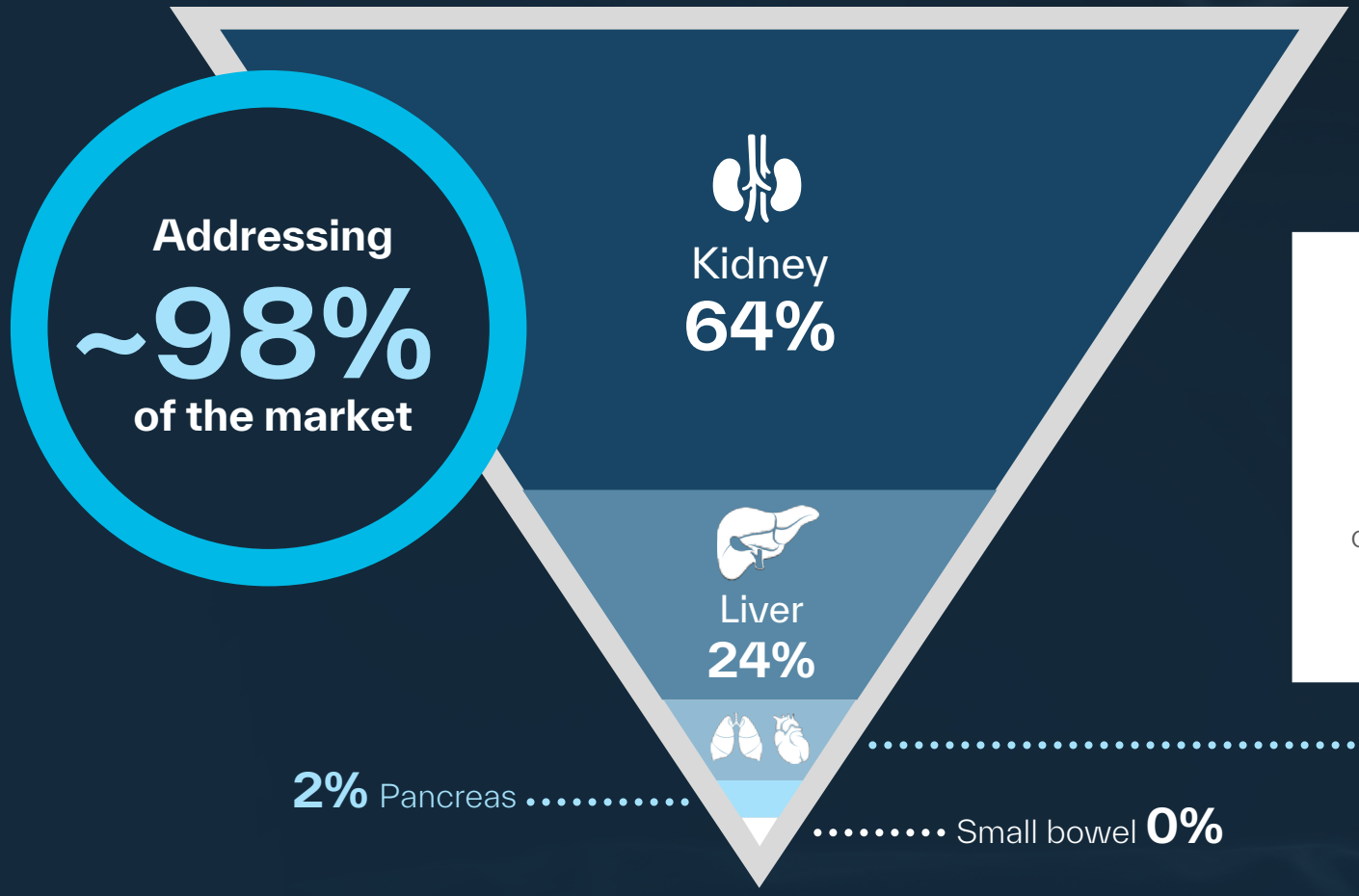
Employees

100

Sales in more than

70 countries

Transplants per organ



Lung & Heart

Lung
4%
of global market
(~6,700)

XVIVO's addressable market in thoracic organs.
10%

Heart
6%
of global market
(~8,300)

XVIVO

XVIVO

Our technology saves organs, so others can save lives

Our offer: We enable safe use of more organs

We increase the availability of organs

We improve organ preservation

We improve organ function and survival

Market & trends

Dag Andersson, CEO

Organ utilization rates

Utilization rate 2019 global averages

XVIVO

Organ utilization must increase

The hurdles

Low utilization of donated organs from **DBD**[1] donors

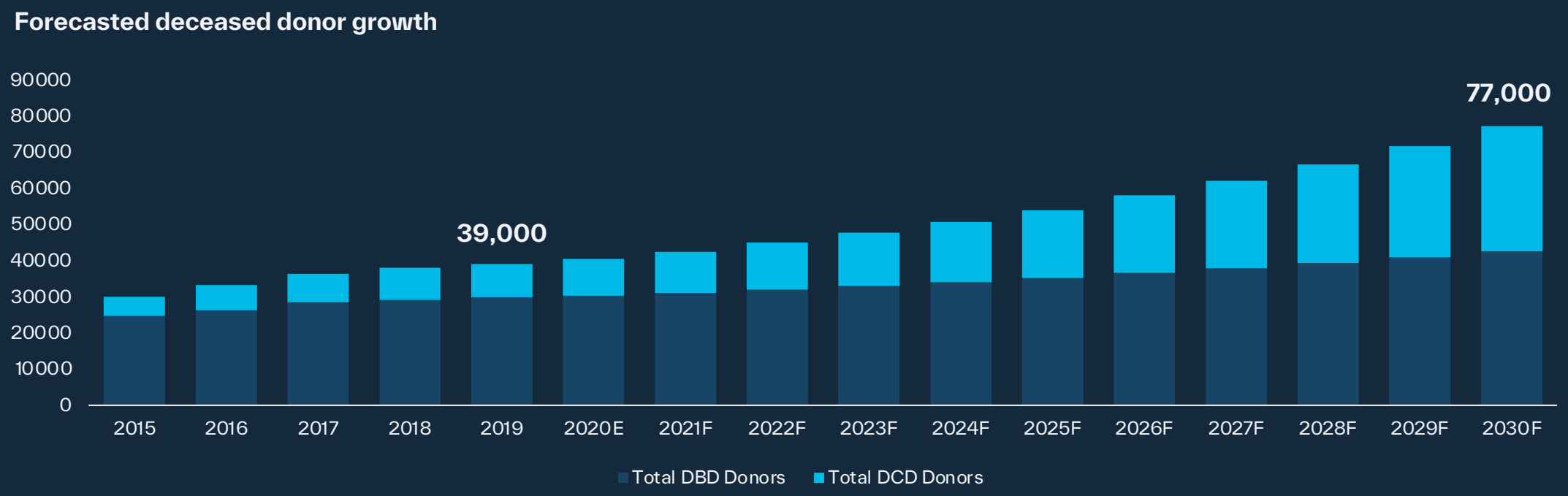
Low or no use of DCD[2] **donors** in thoracic transplantation

Deterioration of organs after retrieval until transplantation

[1] DBD - Donated after brain death

[2] DCD - Donated after circulatory death

Deceased donor growth forecast – All organs



DCD CAGR 2020 - 2030

13 %

DBD CAGR 2020 - 2030

3.4 %

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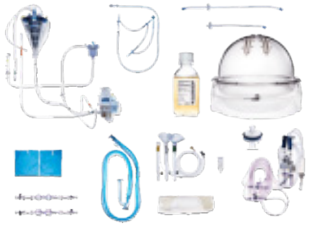
XVIVO is leading the transformation

Lung

MACHINE PERFUSION PLATFORMS

XPS™

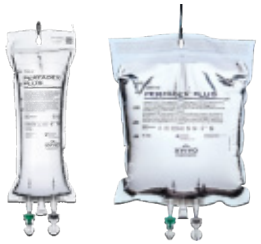
DISPOSABLES FOR MACHINE PERFUSION



XPS DISPOSABLE LUNG KIT™

STEEN SOLUTION™

STATIC PRESERVATION

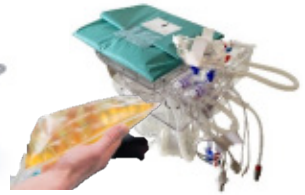


PERFADEX PLUS®

Heart

UNDER EVALUATION IN CLINCAL TRIALS

XVIVO HEART DEVICE™



XVIVO DISPOSABLE HEART SET™*

Kidney

KIDNEY ASSIST TRANSPORT™

KIDNEY ASSIST™

Liver

LIVER ASSIST™

DONOR ASSIST™

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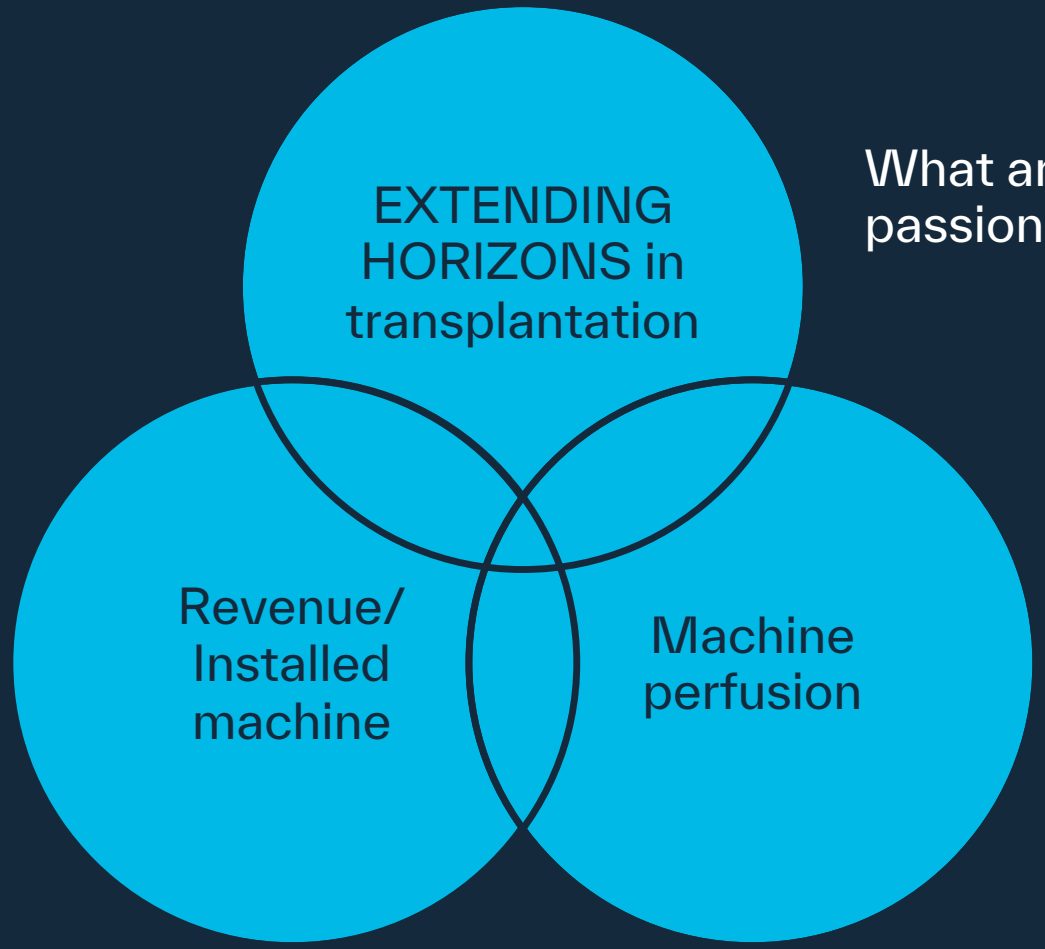
Key take-aways: Market & trends

- A global organ shortage (demand 10x supply)
- Organ utilization must increase
- Machine perfusion will drive increased organ utilization
- XVIVO has the widest machine perfusion offering in the world

Strategy

Dag Andersson, CEO and Kristoffer Nordström, CFO

What are we passionate about?



What drives our ECONOMIC ENGINE?

What shall we be the best in the world at?

Strategy overview 2022-2026

Our purpose	We believe in an extended life for organs. Nobody should die waiting for a new organ.
Our strategic objective	Global leading ‘all organ’ company
Our economic engine	Global leader in machine perfusion – *Revenue/Installed machine*
Our strategic focus areas	Global leader Abdominal (the US)
	Market leading heart preservation system
	Increase penetration of machine perfusion
	Secure all-inclusive reimbursement in key geographies
	China to become our second largest market

Strategic focus areas

Our strategic focus areas 2022-2026

Global leader Abdominal (the US)	Market leading heart preservation system	Increase penetration of machine perfusion	Secure all-inclusive reimbursement in key geographies	China to become our second largest market

Qualifier

The US is the largest transplant market in the world for abdominal

Key activities

- FDA clearance for Kidney Assist Transport and Liver Assist
- Product launches and Go to market plans
- Strengthen the commercial organization

Our strategic focus areas 2022-2026

Global leader Abdominal (the US)	**Market leading heart preservation system**	Increase penetration of machine perfusion	Secure all-inclusive reimbursement in key geographies	China to become our second largest market

Qualifier

Potential to completely transform and set the standard for a new transplant segment

Key activities

- Clinical trials in Europe & the US
- Product launches and Go to market plans
- Preclinical investigations to support extended use of the XVIVO heart system

Our strategic focus areas 2022-2026

Global leader Abdominal (the US)	Market leading heart preservation system	**Increase penetration of machine perfusion**	Secure all-inclusive reimbursement in key geographies	China to become our second largest market

Qualifier

Solving the transplant teams hurdles through forward integration is key to generating increased adoption

Key activities

- Forward integration and new business models
- Drive transplant hub solutions
- Provide digital solutions as an integral part of the value proposition for machine perfusion

Our strategic focus areas 2022-2026

Global leader Abdominal (the US)	Market leading heart preservation system	Increase penetration of machine perfusion	Secure all-inclusive reimbursement in key geographies	China to become our second largest market

Qualifier

Creating conditions for growth rely on stable and clear health economic foundations

Key activities

- Drive and support reimbursement initiatives in key geographies
- Inclusion of health economics to be part of clinical trials
- Collaborations with patient organisations and KOLs

Our strategic focus areas 2022-2026

Global leader Abdominal (the US)	Market leading heart preservation system	Increase penetration of machine perfusion	Secure all-inclusive reimbursement in key geographies	China to become our second largest market

Qualifier

Growth trends suggest China will become the world's largest transplant market within 10-15 years

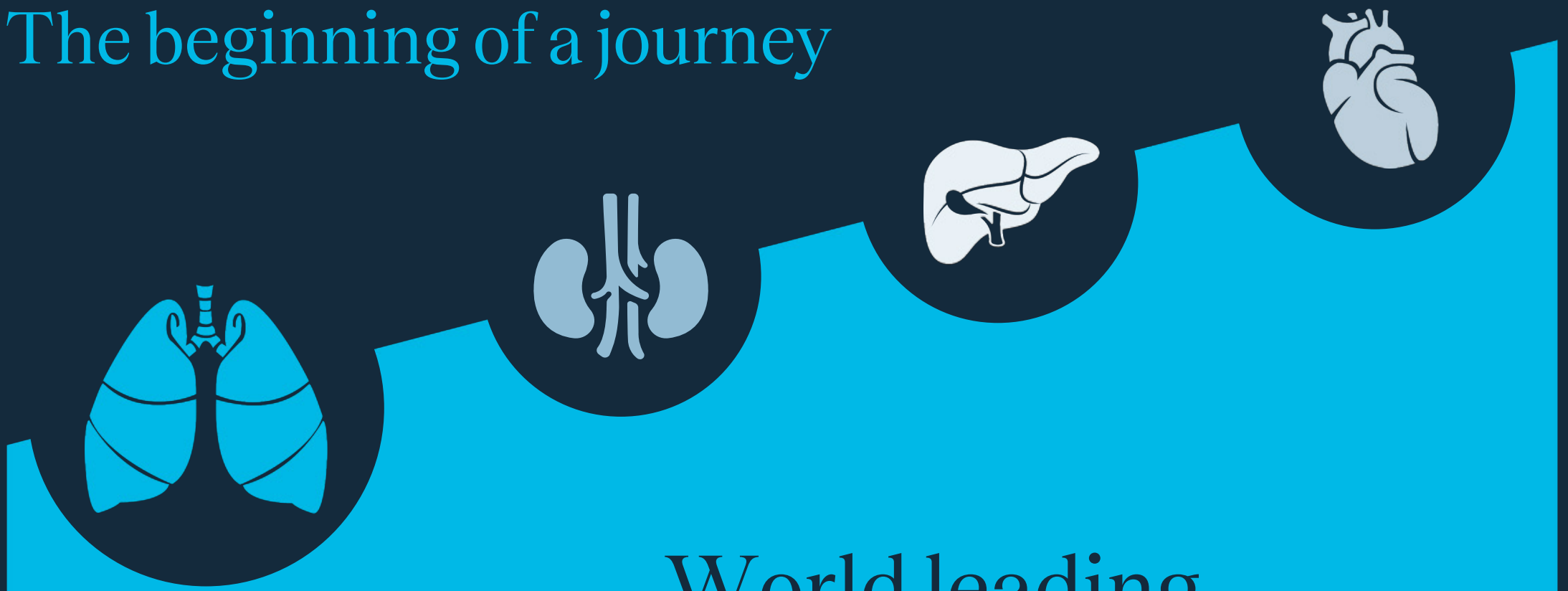
Key activities

- Regulatory strategy to gain approval for key products
- Build KOL and distributor networks
- Build a strong market presence

Financial targets

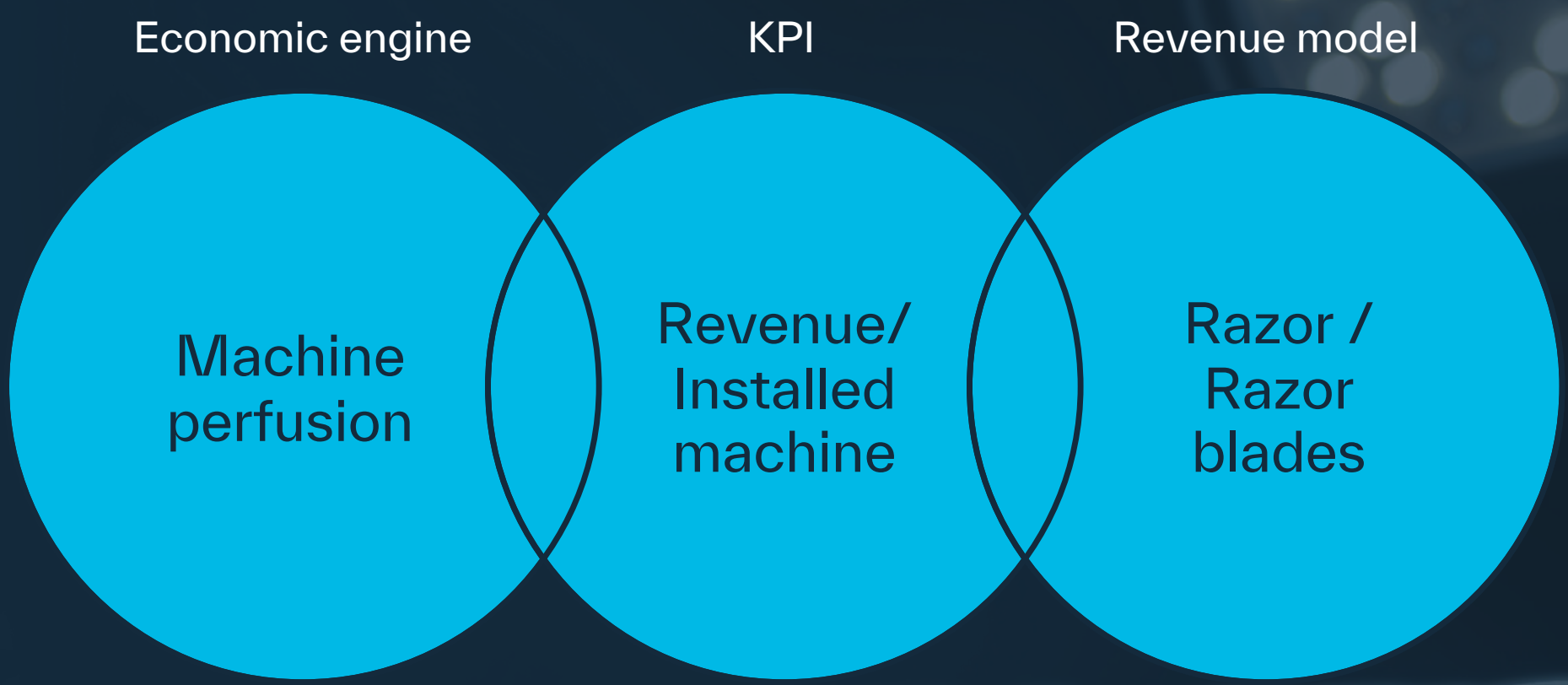
Kristoffer Nordström, CFO

The beginning of a journey

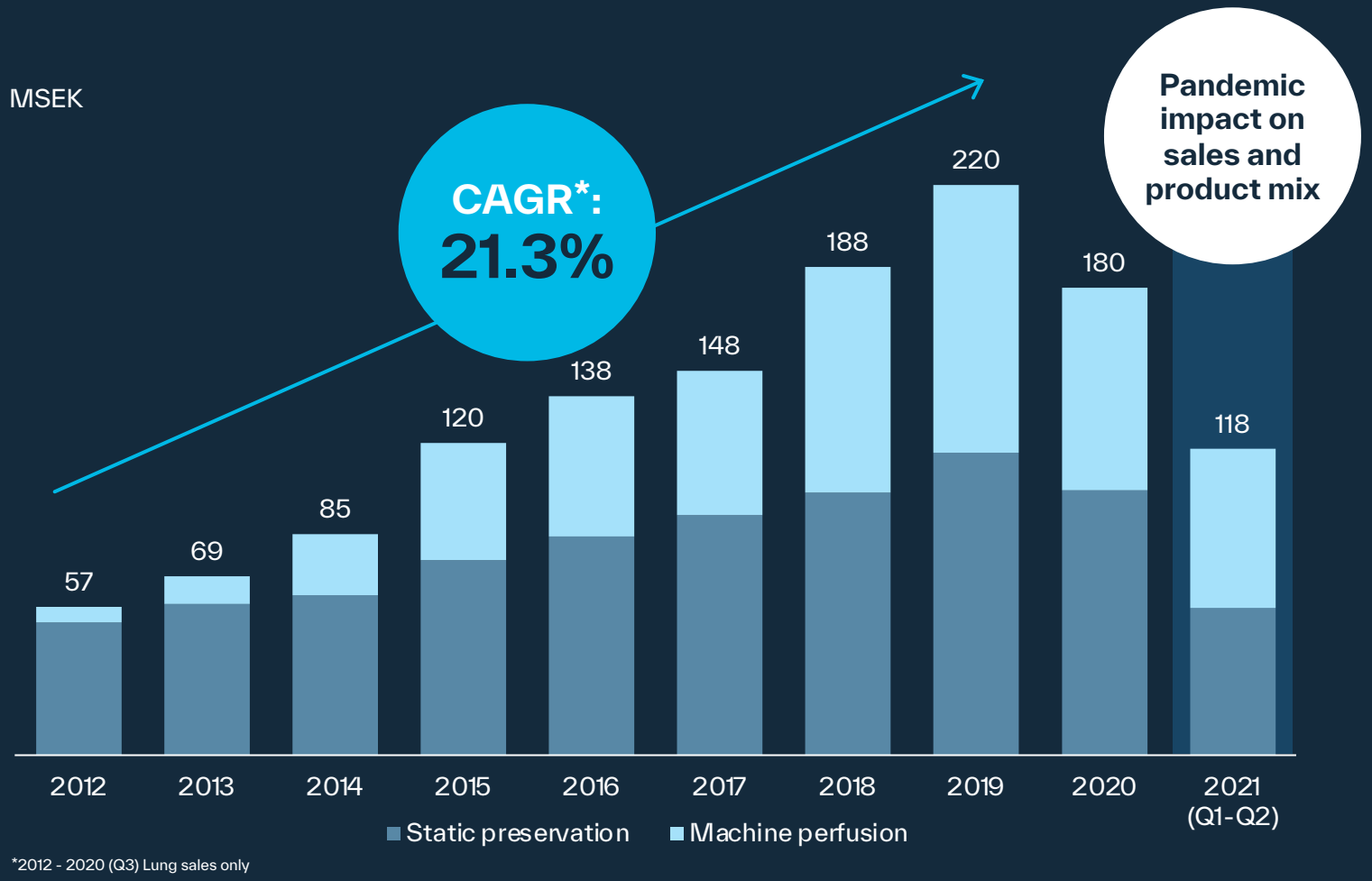


World leading –
20 years of experience

Our business model



Strong double-digit growth



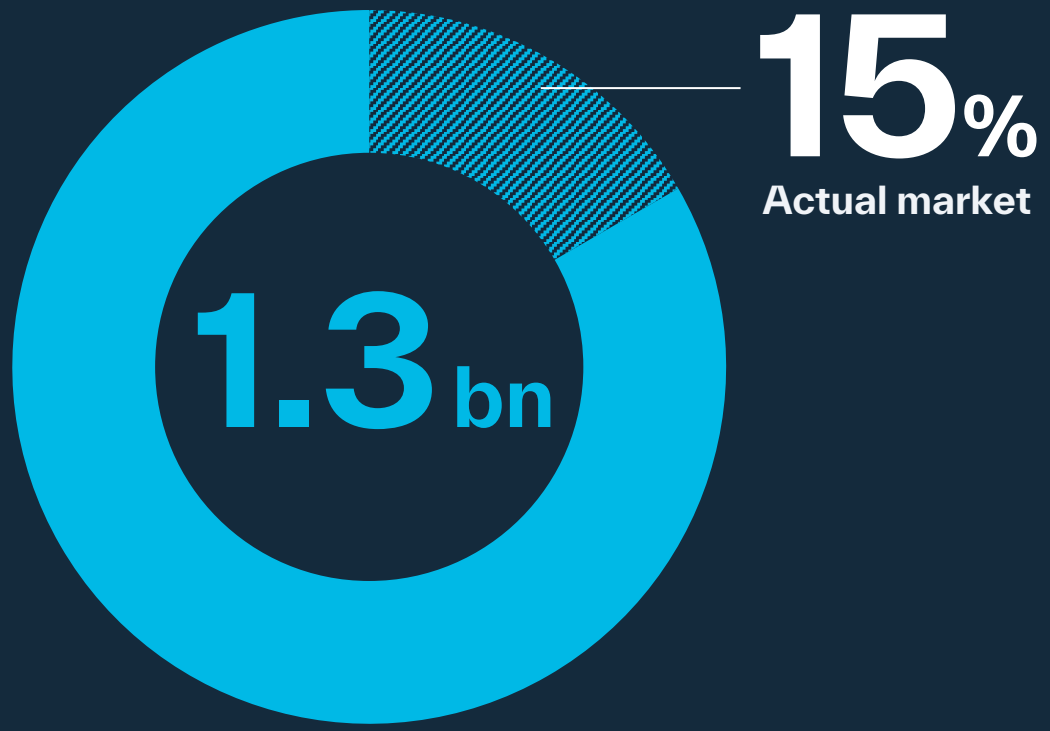
*2012 - 2020 (Q3) Lung sales only

Lung sales

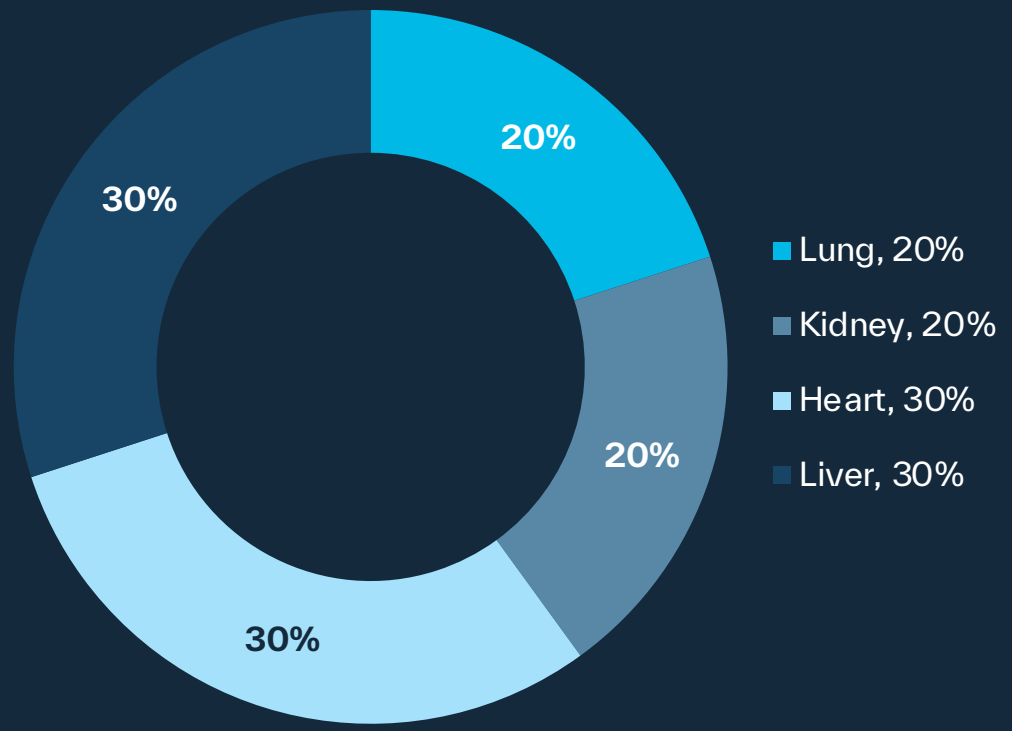
- Static preservation has historically grown with the market
- Machine perfusion has shown a **CAGR of 42 %** until 2019

Market value - Machine perfusion

Total market value potential of machine perfusion* (USD)



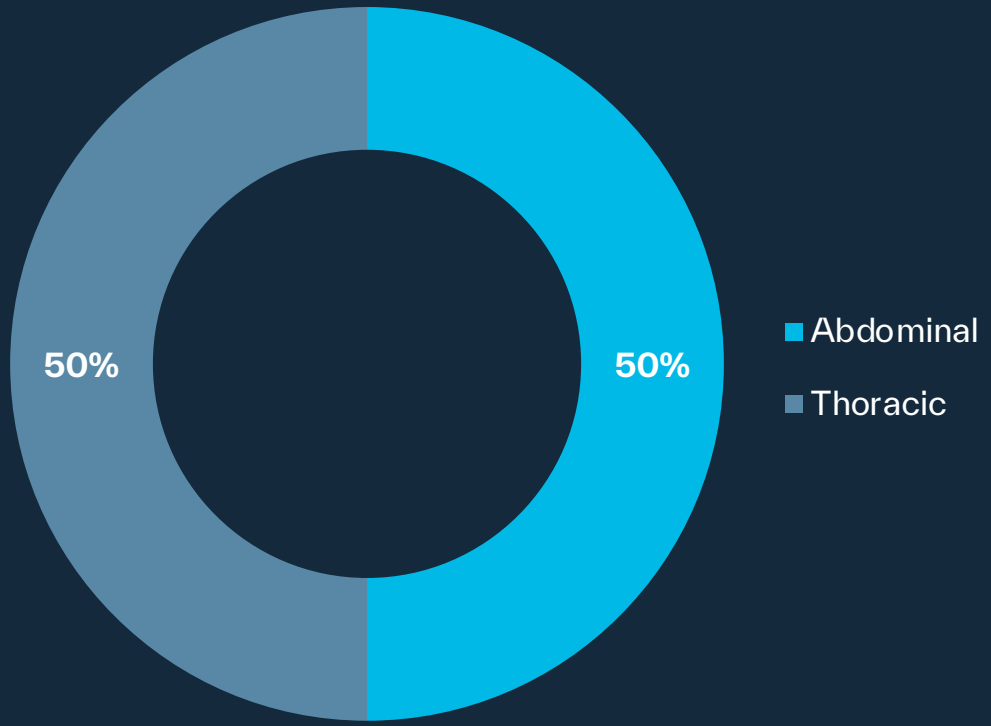
Market potential value split



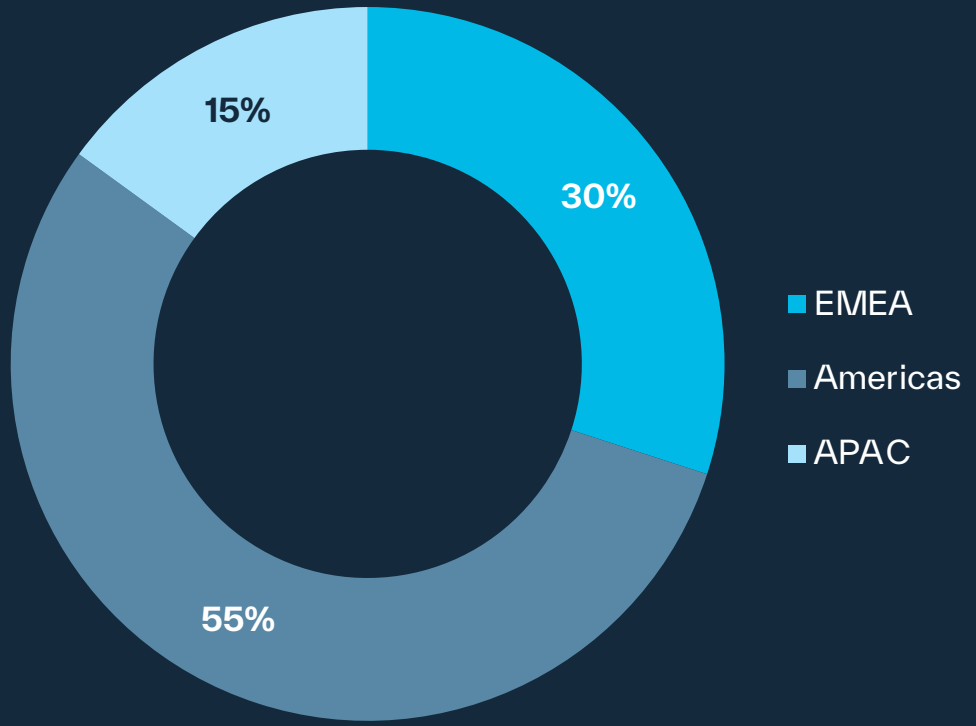
*Deceased donors. Solutions and disposables only (no machines or static preservation)

2026 – Main assumptions: Sales

Sales by business area



Sales by region



2026 – Profitability targets

EBIT (%)

20

EBITDA (%)

30

Key take-aways: Strategy

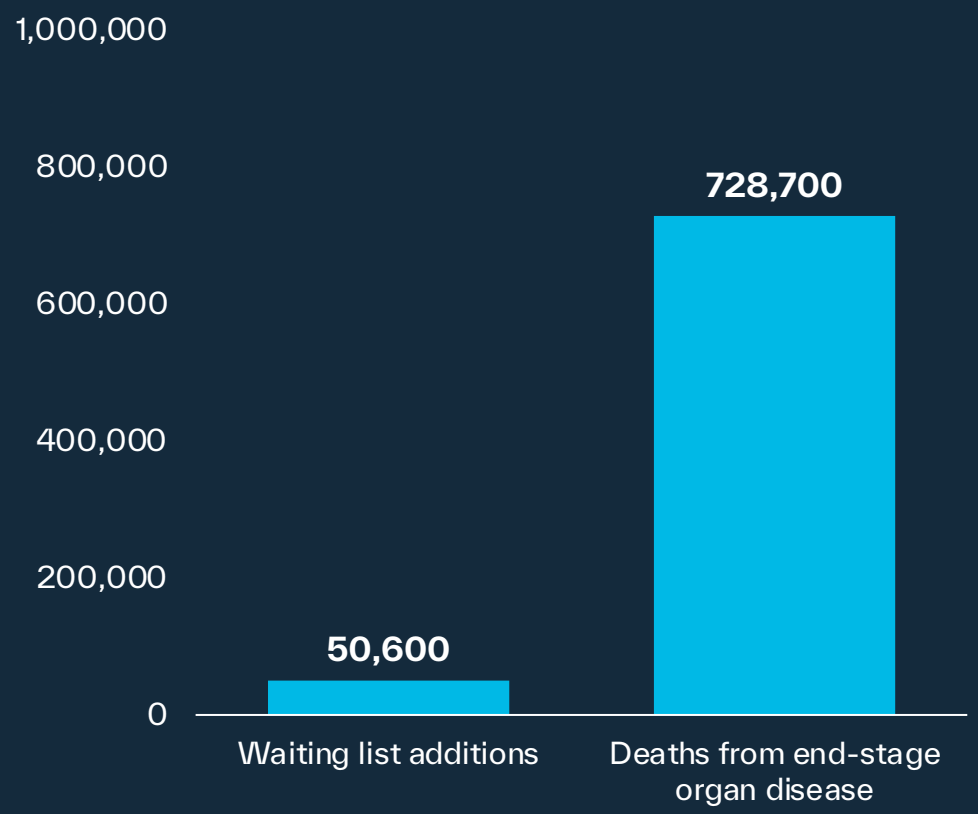
- Five strategic focus areas will make XVIVO become the global leading ‘all organ’ company
- Machine perfusion is what we are best in the world at and our economic engine
- Revenue model for lung will be applied also on kidney, liver and heart
- 2026 profitability targets of 20% EBIT and 30% EBITDA

Health economics

Johan Holmström, CCO

Health benefit, the true potential of organ transplantation

- The waiting list situation fails to capture the true magnitude of the organ shortage
- The possibility to replace organs and tissues on demand could generate health benefits on level with curing cancer



Giwa S, Lewis JK, Alvarez L, et al. The promise of organ and tissue preservation to transform medicine. Nat Biotechnol. 2017;35(6):530-542.

Health benefits to drive reimbursement

- Clinical evidence and national guidelines as a foundation
- Publications, (e.g. the recent NEJM publication on HMPO2)
- Perform clinical investigations on national level
- Confirm and recommend clinical guidelines, e.g. NICE
- Clinical guidelines to support financial guidance and recommended reimbursement

Overview – Reimbursement

XVIVO is directly or indirectly involved in several initiatives that will open up reimbursement in EU countries for machine perfusion

- The US covered through medicare / aid and private insurance
- Asia & China: No nationwide reimbursement for specific procedures or use of certain medical devices currently exists
- Transplantation as intervention is reimbursed in EU countries
- Clinical practice of machine perfusion is only reimbursed in selective EU countries
- Positive development on how to increase funding for the clinical practices that drives increase of lifesaving transplants
- We see a very positive development in France, Belgium, the Netherlands, Germany and the UK

NICE gives support for EVLP (the UK)

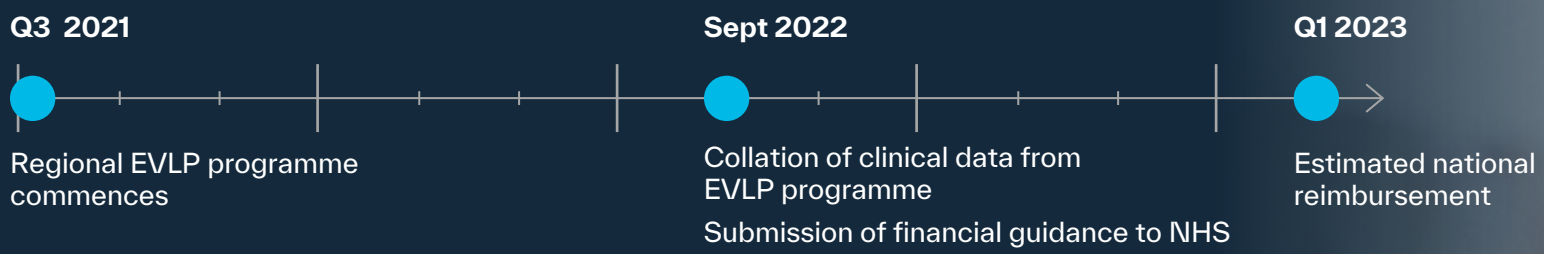
In May, XVIVO announced that The National Institute for Health and Care Excellence (NICE), had issued interventional procedure guidance recommending the use of Ex Vivo Lung Perfusion (EVLP) for preservation of lungs

2021

- Guidelines published in May
- National hub model

Next steps

- XVIVO has initiated a process for reimbursement based on NICE guidelines
- Collation of clinical evidence on EVLP in the UK
- Business case to be submitted to NHSBT
- Estimated reimbursement Q1 2023



France - Successful case

Both EVLP (lung) and machine perfusion for kidney is granted reimbursement

- Significant increase in available organs and improved transplant outcomes
- Health care cost savings compared to number of renal services

Reimbursement for machine perfusion of liver – on its way

- XVIVO in close collaboration
- XVIVO Liver Assist, HOPEX trial, 8 centres

Netherlands – Positive news!

Kidney machine perfusion reimbursed successfully

NEWS! EVLP will be granted from January 2022

NEWS! Liver machine perfusion from January 2022

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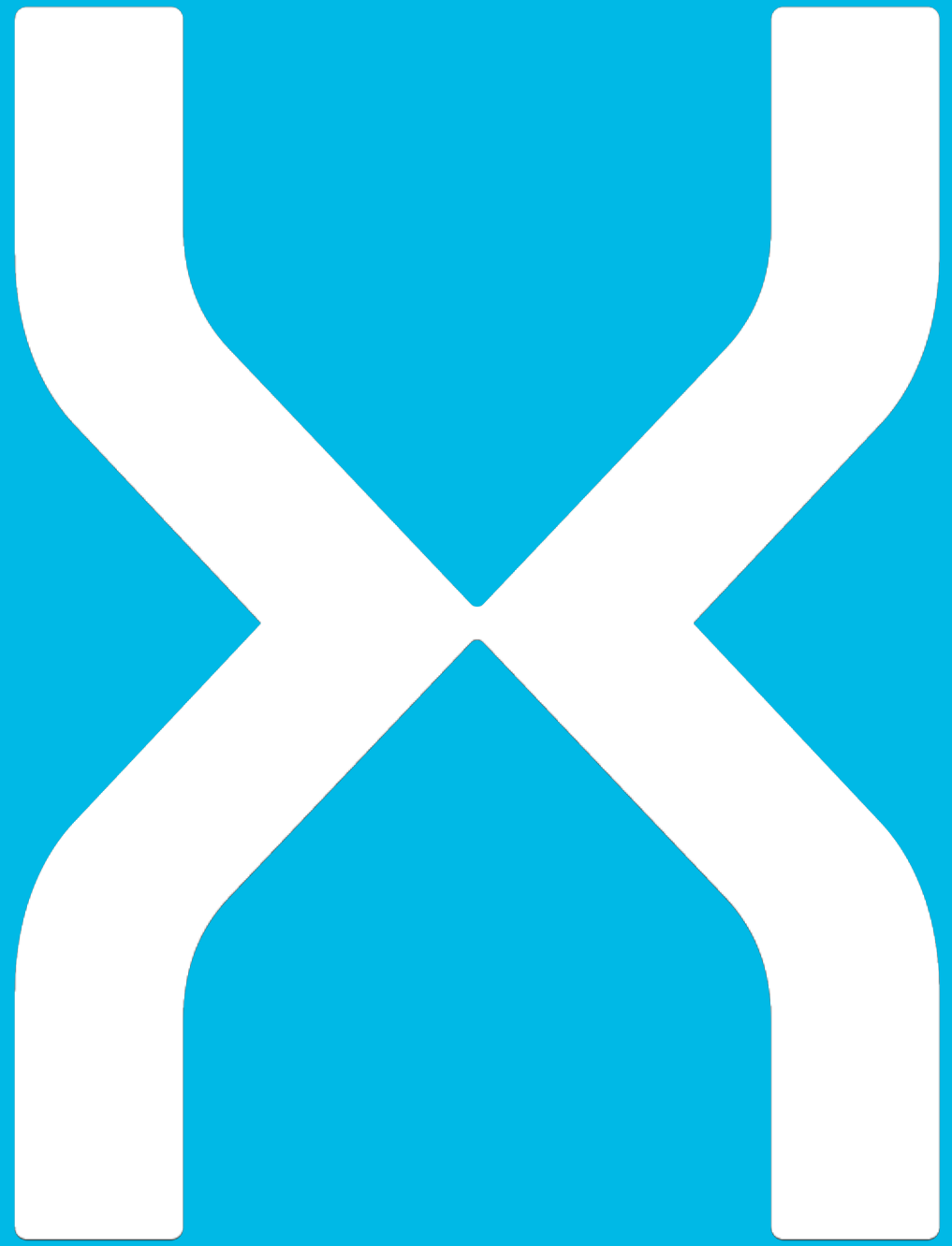
Key take-aways: Health economics

- Clear health economic benefit from transplantation
- XVIVO is supporting several research initiatives and projects to drive reimbursement and funding
- Clinical evidence is a key driver
- Debate is no longer focusing on the clinical benefits of machine perfusion but rather on funding

Q&A

Break



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16.55	- 17.00	Thank You	Dag Andersson, CEO

Heart

Andreas Wallinder M.D., Ph.D., CMO

Overview: Heart

The market

Key facts

No of transplants*
- 8,600

Organ utilization rate
- 30%

Active clinics
- 350

Main market challenges
- Growing need for transplantation (incl. use of DCD)
- Transport time is a limited factor

XVIVO today

Market presence

XVIVO products
- XVIVO heart preservation system (in clinical trials for regulatory purpose)

Clinical trials
- NIHP Trial in Europe
- NIHP Trial in the US (planned)
- NIHP Trial in ANZ
- NIHP Trial in Lund (Sweden)

Where Heart supports our strategy

Strategic focus areas 2022 – 2026

- Market leading heart preservation system
- Increase penetration of machine perfusion
- Secure all-inclusive reimbursement in key geographies

*2019 figures

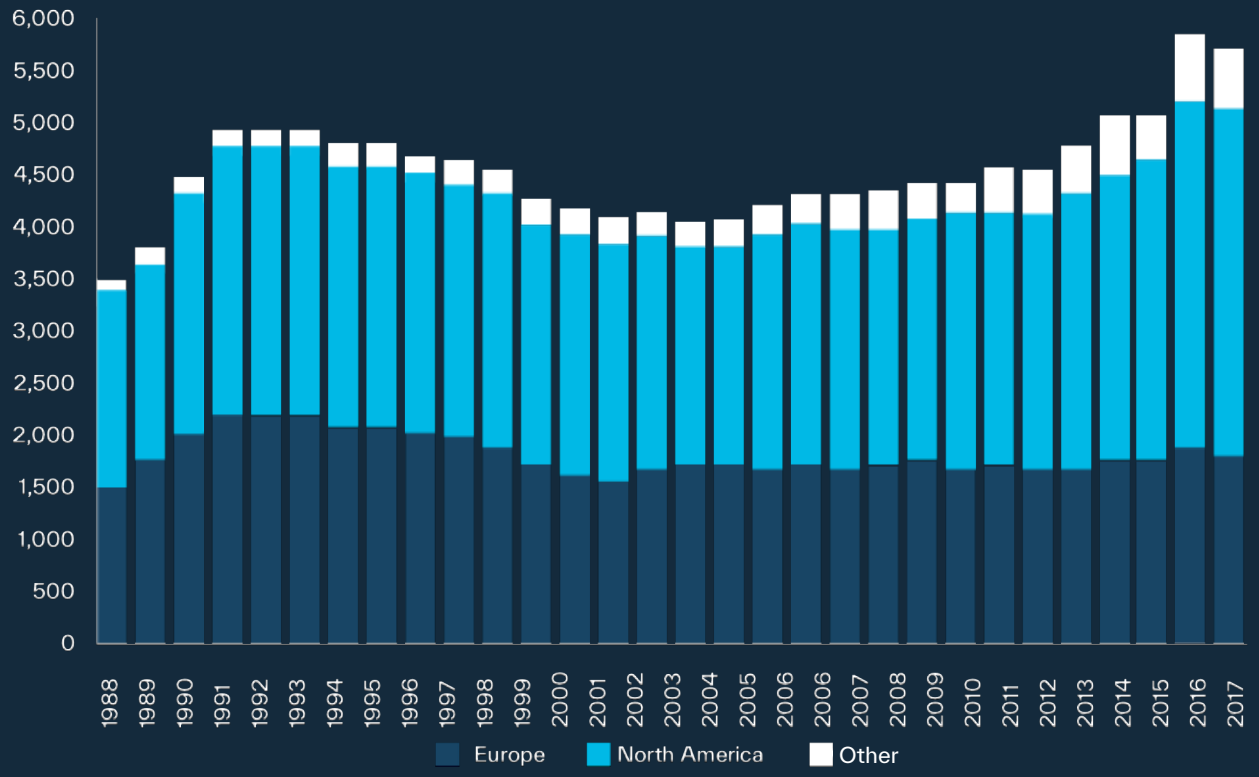
Heart failure

- Heart failure is a chronic illness with a median survival of 2 years after diagnosis
- Once heart failure progresses to the final stage, patients experience poor quality of life, high symptom burden and face a median life expectancy of only 6–12 months
- Heart disease is the leading cause of death globally
- At the final stage of heart failure transplantation is a life saving treatment available for a small minority of the patients

Groenewegen A, Epidemiology of heart failure. Eur J Heart Fail. 2020;22(8):1342-1356.

Heart transplantation today

Adult and pediatric heart transplants
Number of transplants by year and location



Khush KK et al. J Heart Lung Transplant. 2020 Jan;39(1):91]. J Heart Lung Transplant. 2019;38(10):1056-1066. doi:10.1016/j.healun.2019.08.004

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Donor heart standard of care

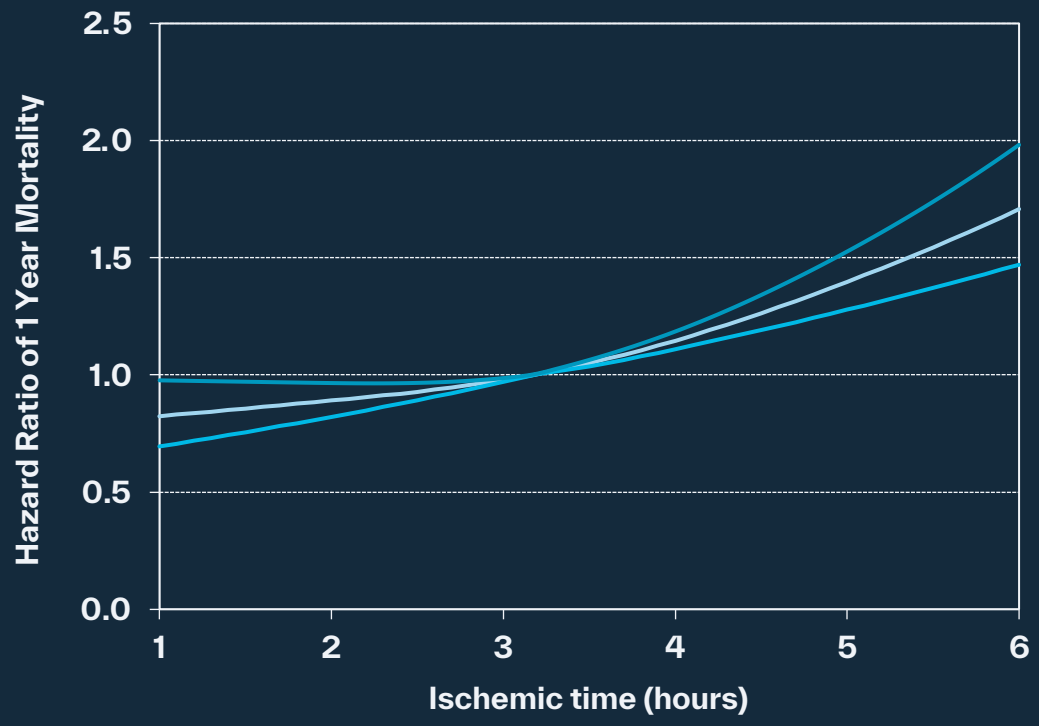
The donor heart it is flushed with a cold solution that arrests the activity before explant

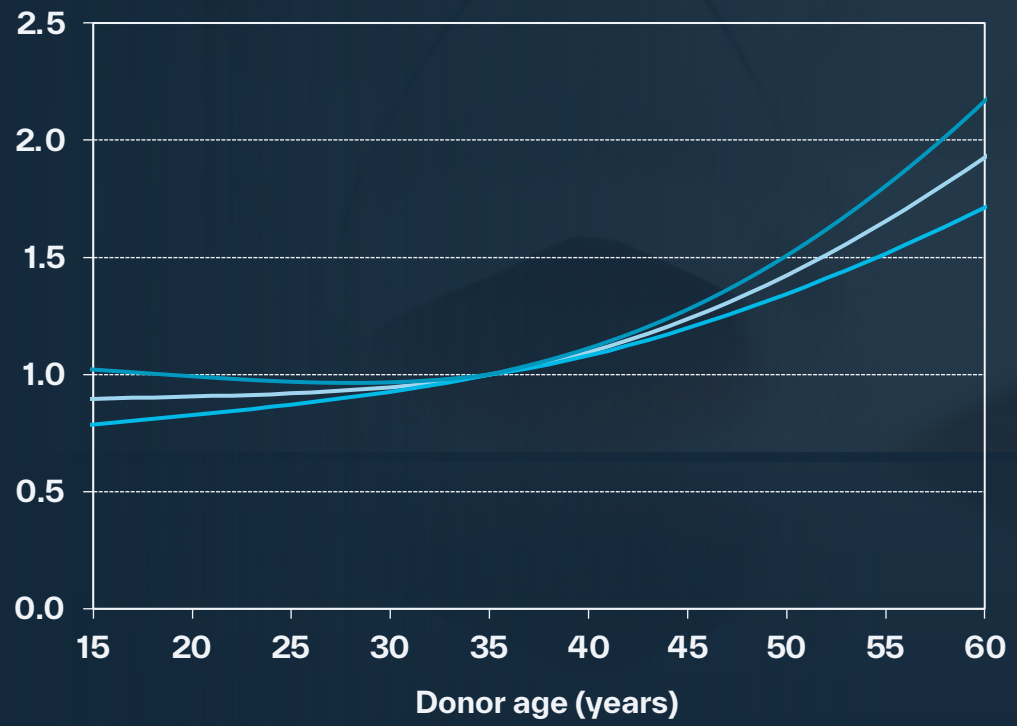
During the first 50 years of heart transplant donor hearts have been placed in plastic bags with cold solution and placed on ice in a cooler during transport

Once the heart is arrested the absence of circulation and oxygen induces progressive degradation of the tissue – Ischemic injury

When the heart is restarted in the recipient any ischemic injury translates into impaired heart function

Impact of ischemic time





Khush KK et al. J Heart Lung Transplant. 2020 Jan;39(1):91]. J Heart Lung Transplant. 2019;38(10):1056-1066. doi:10.1016/j.healun.2019.08.004


2h
3h
6h
ISLAND
SVERIGE
NORGE
FINLAND
DANMARK
POLEN
TYSKLAND
FRANKRIKE
SPANIEN
PORTUGAL
IRLAND
UKRAINA
TURKIET
GREKLAND
BULGARIEN
RUMÄNIEN
SERBIEN
KIRGIZISTAN
TADZJIKISTAN
AFGHANISTAN

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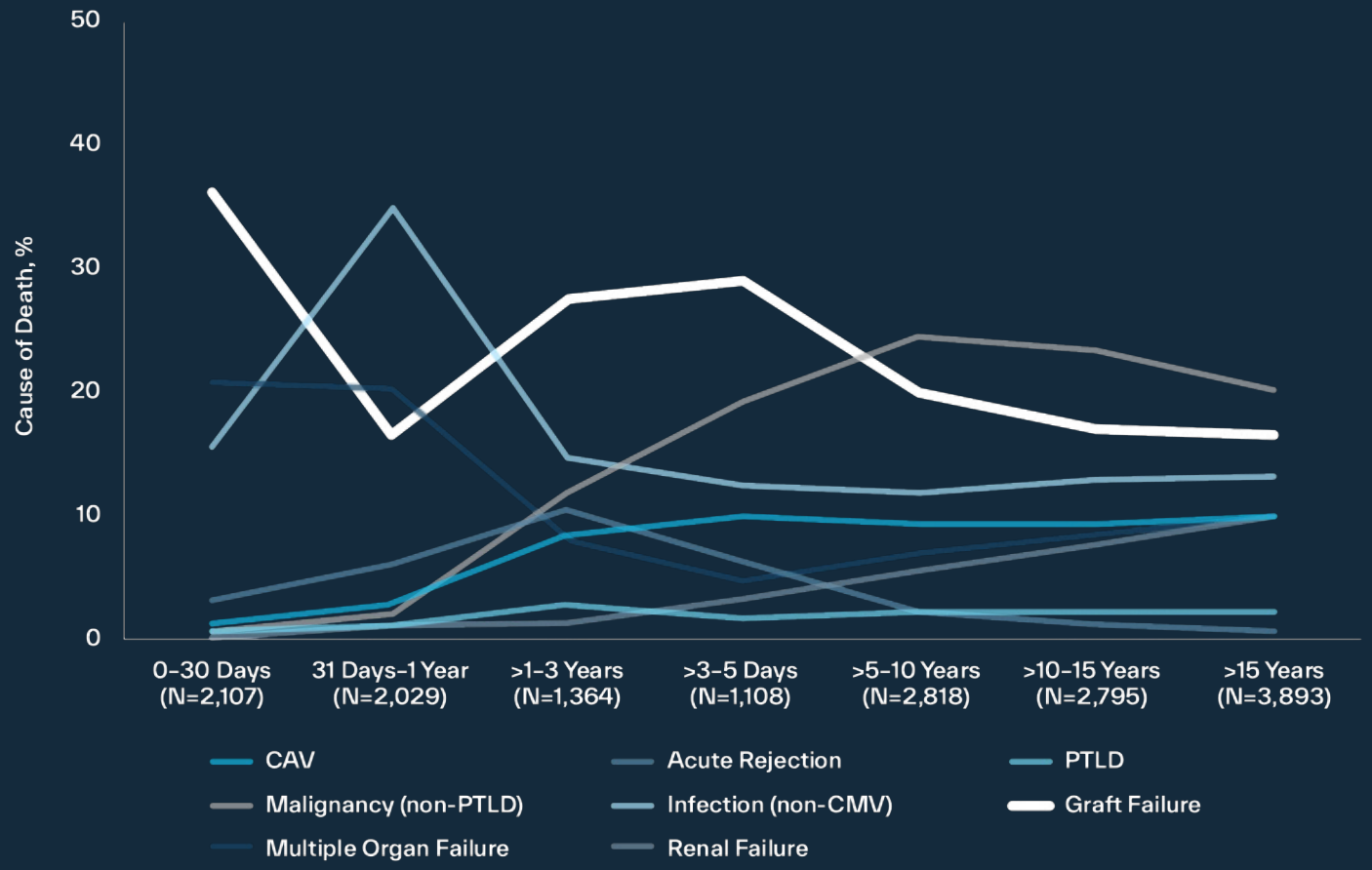
Early causes of death after heart transplantation

- Failure of the transplanted heart is the leading cause of death after transplantation
- Injury to the donor heart during transport on ice is causing poor function in the recipient



JHLT. 2019 Oct; 38(10): 1015-1066

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Challenges in donor heart preservation

Ischemic injury to the donor heart during transport on ice is causing poor function after transplantation in the recipient.

The transport time / Ischemic time is ideally limited to 4 hours or less.

There is need for a better preservation method for donor hearts

- Surgical teams turn down more than 70% of donor hearts today
- Better preservation could improve post-transplant results, increase the use of donor hearts and allow for safe, long distance donor heart transports

The evolution of non-ischemic heart preservation (NIHP)

From cold static storage on ice

To Continuous oxygenated perfusion with a tailored solution

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Preclinical proof of concept studies demonstrates

- Reduced ischemic injury > Better organ quality after transplant
- Longer preservation time possible (24 hours)
- Allowed long term survival in Pig to Primate transplant (Xeno)

Non-ischemic heart preservation (NIHP)

XVIVO Heart System

Creates an optimal environment by supplying the resting heart with important substances in an oxygenated solution.

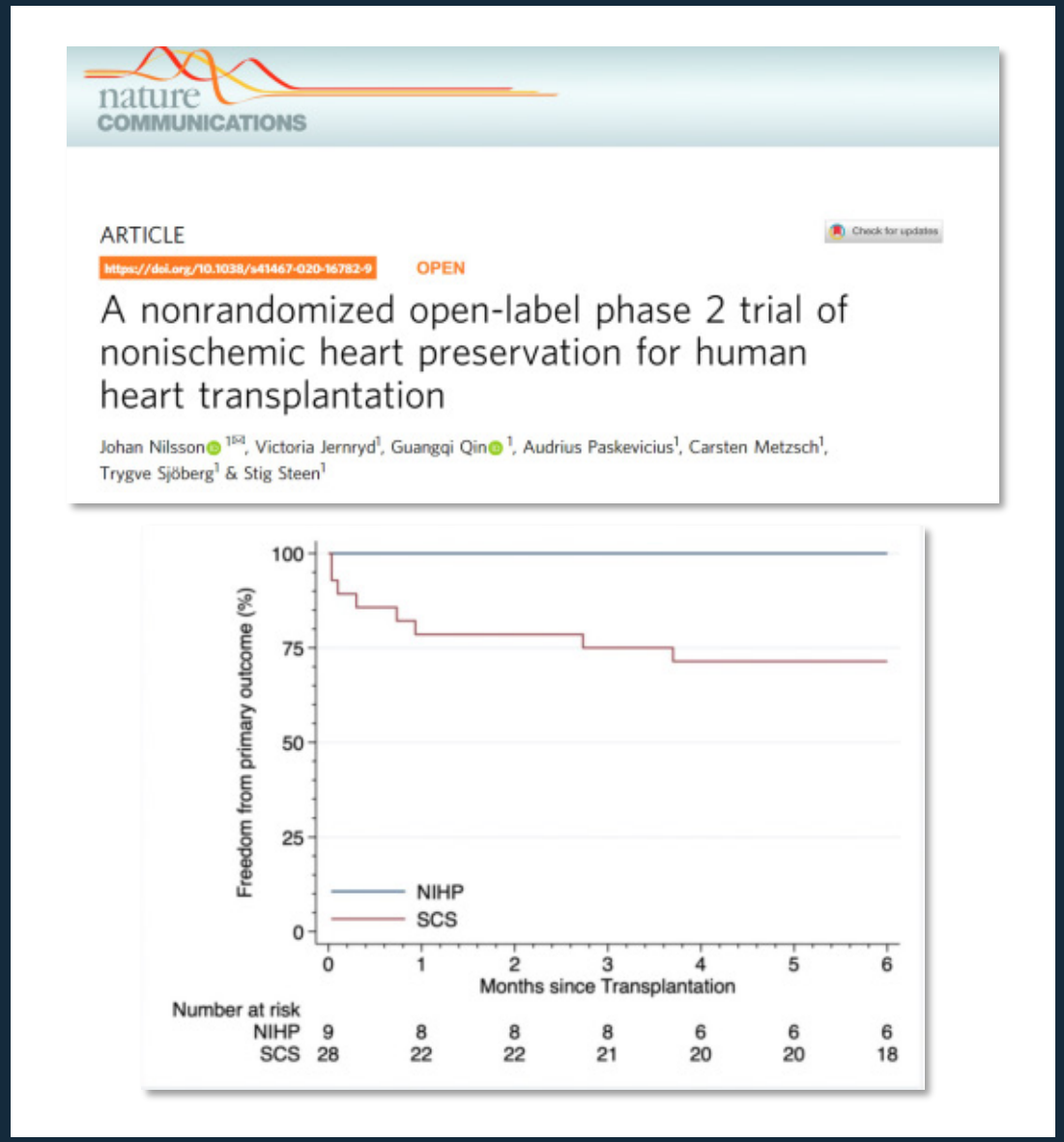
Device
A portable device used to preserve hearts using non-ischemic cold perfusion.

Solution
Buffered and supplemented solution for flushing of the donor heart and perfusion during transport.

Disposable
A single-use set to be installed and connected to the heart machine.

First in human study

- Sponsor: Skåne University Hospital, Lund
- Initial results published 2020
- Interim results presented at the European Society of Organ Transplantation (ESOT) Meeting Milan September 2021
- 100% 6-month survival without graft failure
- Recruitment ongoing



NIHP Australia / New Zealand

- Sponsor: Alfred Health, Melbourne, Australia
- Explore extended transport times of donor hearts with NIHP (6-8 hours)
- First hearts with extended ischemic times successfully transplanted

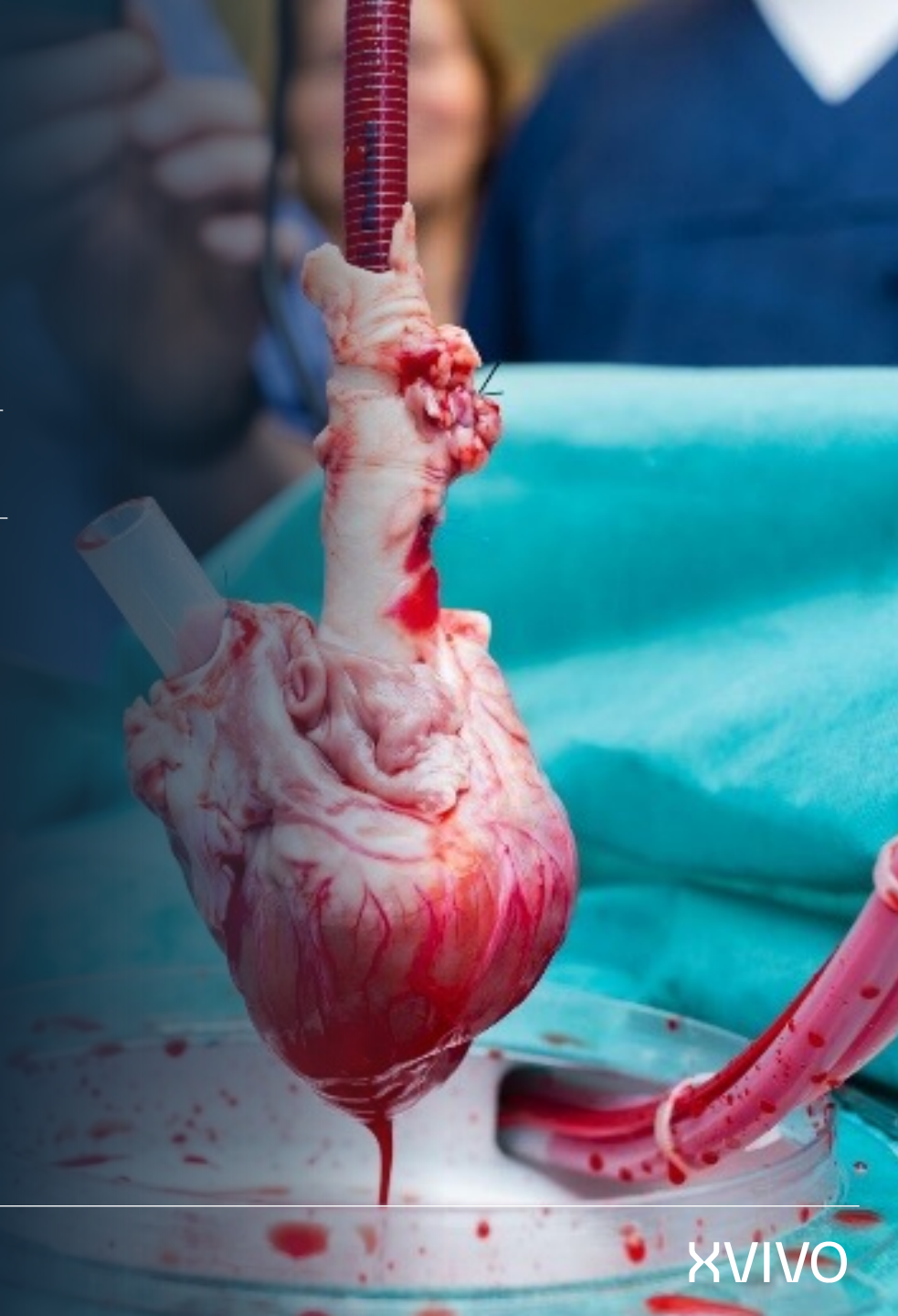
XVIVO sponsored studies

(NIHP EU)

- First patient reported December 2020
- Recruiting at 6 sites
- Standard donor hearts and transport times less than 6 hours

(NIHP US)

- Ongoing discussion with FDA in preparation for IDE submission
- Additional preclinical test ongoing in September and October
- IDE submission to FDA before end of the year
- Study start 2022



Key take-aways: Heart

XVIVO's game changing heart preservation technology has potential to:

- Improve outcome after heart transplantation by replacing the cold, ischemic storage on ice used today with oxygenated perfusion of the donor heart with an optimal solution
- Safely extend the time a donor heart can be outside of the body allowing for long distance transports, optimal allocation and removal of detrimental pressure on surgical teams
- Increase utilization of extended criteria donor hearts

The European NIHP study -Non-ischemic heart preservation

Prof. Filip Rega, The University Hospitals Leuven

XVIVO

Non-Ischemic Heart Preservation

Capital Markets Day

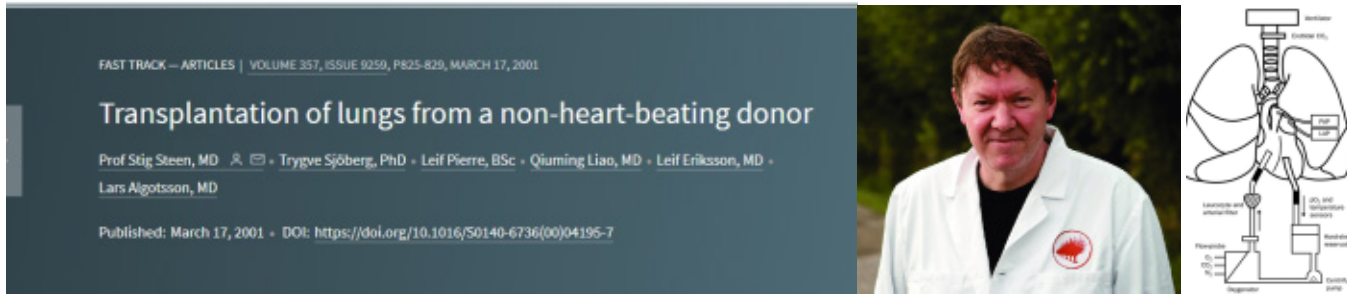
November 23, 2021

Filip Rega, MD, PhD

Head of Clinic, University Hospitals Leuven, Belgium
Professor, Cardiovascular Sciences, KU Leuven, Belgium
Director of the Leuven Surgical Heart Transplant Program
Principal Investigator NIHP Trial

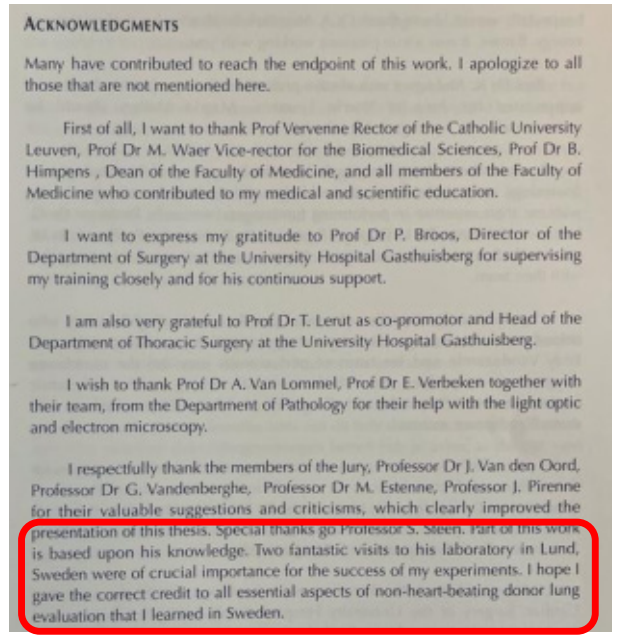
Leuven – NIHP

THE LANCET



Long-term Preservation With Interim Evaluation of Lungs From a Non-Heart-Beating Donor After a Warm Ischemic Interval of 90 Minutes

Filip R. Rega, MD, Nicole C. Jannis,* Geert M. Verleden, MD, PhD,† Toni E. Lerut, MD, PhD,‡ and Dirk E. M. Van Raemdonck, MD, PhD*‡*



ACKNOWLEDGMENTS

Many have contributed to reach the endpoint of this work. I apologize to all those that are not mentioned here.

First of all, I want to thank Prof Vervenne Rector of the Catholic University Leuven, Prof Dr M. Waer Vice-rector for the Biomedical Sciences, Prof Dr B. Himpens , Dean of the Faculty of Medicine, and all members of the Faculty of Medicine who contributed to my medical and scientific education.

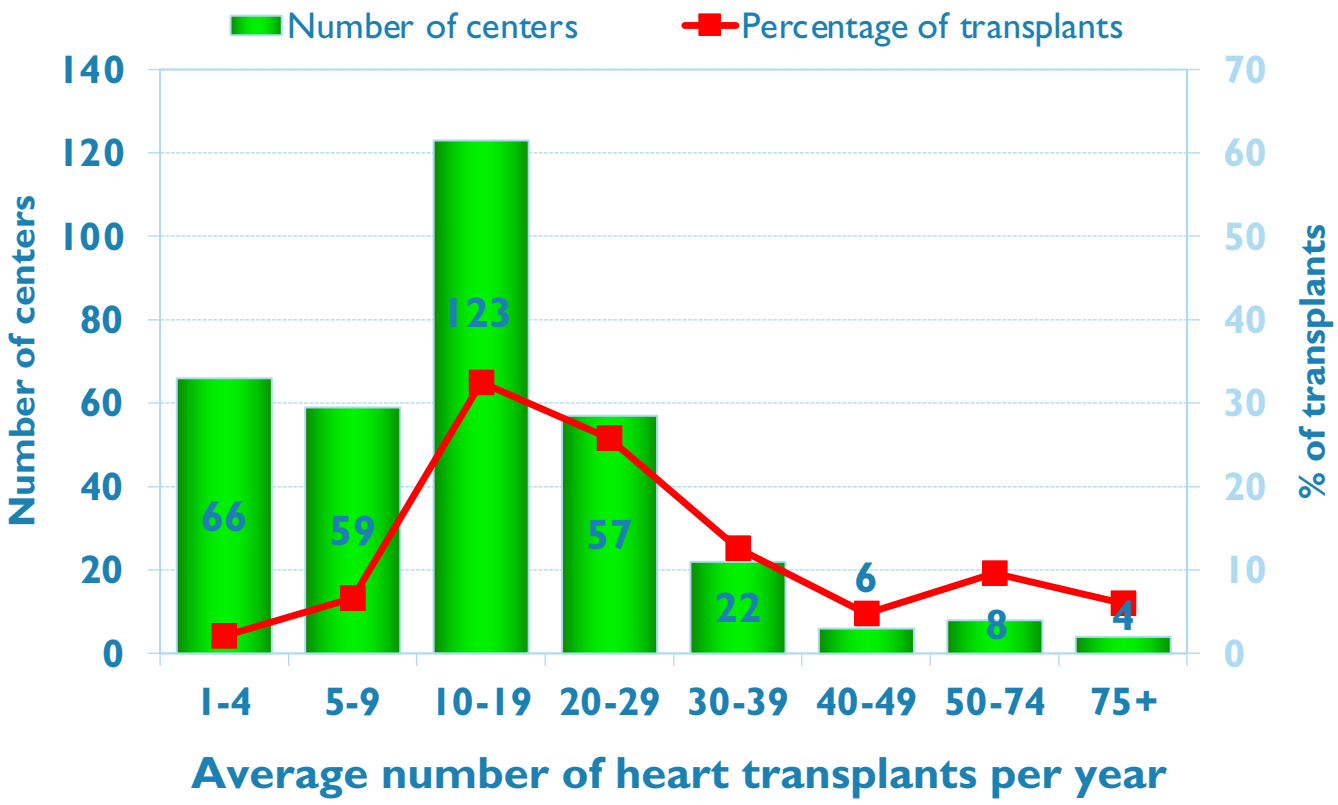
I want to express my gratitude to Prof Dr P. Broos, Director of the Department of Surgery at the University Hospital Gasthuisberg for supervising my training closely and for his continuous support.

I am also very grateful to Prof Dr T. Lerut as co-promotor and Head of the Department of Thoracic Surgery at the University Hospital Gasthuisberg.

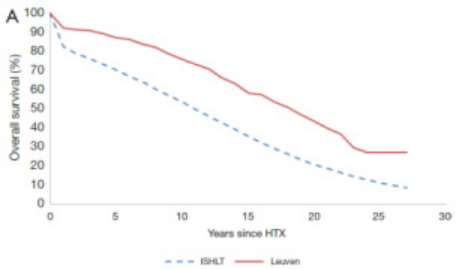
I wish to thank Prof Dr A. Van Lommel, Prof Dr E. Verbeken together with their team, from the Department of Pathology for their help with the light optic and electron microscopy.

I respectfully thank the members of the Jury, Professor Dr J. Van den Oord, Professor Dr G. Vandenberghe, Professor Dr M. Estenne, Professor J. Pirenne for their valuable suggestions and criticisms, which clearly improved the presentation of this thesis. Special thanks go Professor S. Steen. Part of this work is based upon his knowledge. Two fantastic visits to his laboratory in Lund, Sweden were of crucial importance for the success of my experiments. I hope I gave the correct credit to all essential aspects of non-heart-beating donor lung evaluation that I learned in Sweden.

Leuven – NIHP



How to obtain and maintain favorable results after heart transplantation: keys to success?



Leuven – NIHP

European Journal of Cardio-Thoracic Surgery 00 (2021) 1–7
doi:10.1093/ejcts/ezab139

ORIGINAL ARTICLE

Cite this article as: Vandendriessche K, Tchana-Sato V, Ledoux D, Degezelle K, Rex S, Neyrinck A et al. Transplantation of donor hearts after circulatory death using normothermic regional perfusion and cold storage preservation. Eur J Cardiothorac Surg 2021; doi:10.1093/ejcts/ezab139.

Transplantation of donor hearts after circulatory death using normothermic regional perfusion and cold storage preservation

Katrien Vandendriessche [a,b,*], Vincent Tchana-Sato [c], Didier Ledoux [d], Karlien Degezelle [a], Steffen Rex [b,e], Arne Neyrinck [b,e], Ina Jochmans [f,g], Diethard Monbaliu [f,g], Christophe Vandenbriele [b,h], Johan Van Cleemput [b,h], Bart Meyns [a,b] and Filip Rega [a,b]

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[b] Department of Cardiovascular Sciences, Catholic University Leuven, Leuven, Belgium
[c] Department of Cardiothoracic Surgery, University Hospital Liège, Liege, Belgium
[d] Department of Anesthesiology and Intensive Care, University Hospital Liège, Liege, Belgium
[e] Department of Anesthesiology, University Hospitals Leuven, Leuven, Belgium
[f] Department of Abdominal Transplantation, University Hospitals Leuven, Leuven, Belgium
[g] Transplant Research Group, Department of Microbiology, Immunology, and Transplantation, Catholic University Leuven, Leuven, Belgium
[h] Department of Cardiology, University Hospitals Leuven, Leuven, Belgium

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Key question

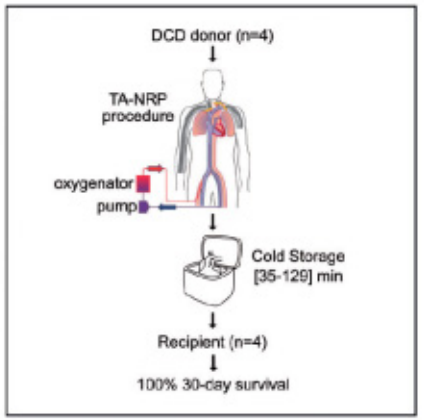
Is cold storage (CS) safe and effective for Donation after circulatory death (DCD) hearts following thoraco-abdominal normothermic regional perfusion (TA-NRP)?

Key finding(s)

Four DCD TA-NRP hearts preserved using CS for up to 129 min were successfully transplanted.

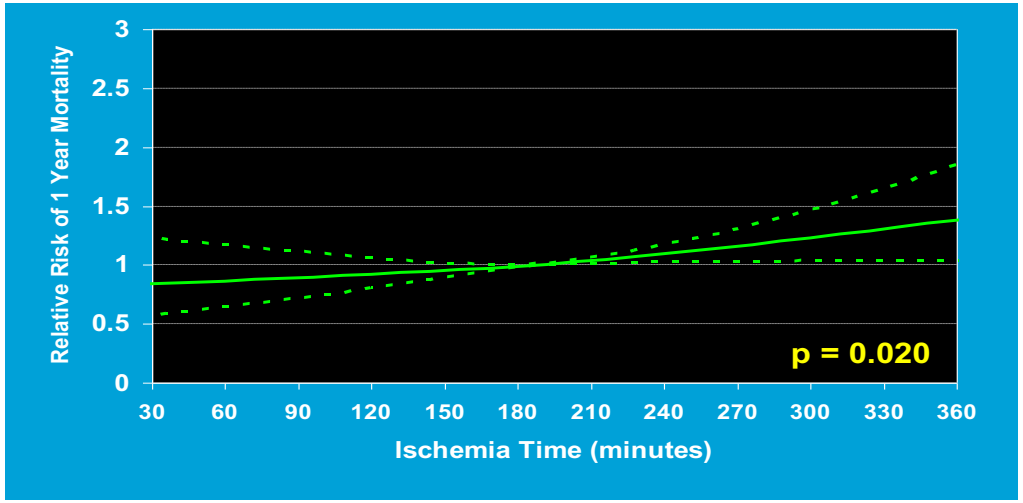
Take-home message

DCD hearts transplanted using TA-NRP and CS for up to 129 min could be a safe and effective way to expand the donor heart pool.



NIHP

- SCS is the standard method for organ preservation
- Limitations SCS
  - Prolonged preservation leads to tissue damage



NIHP

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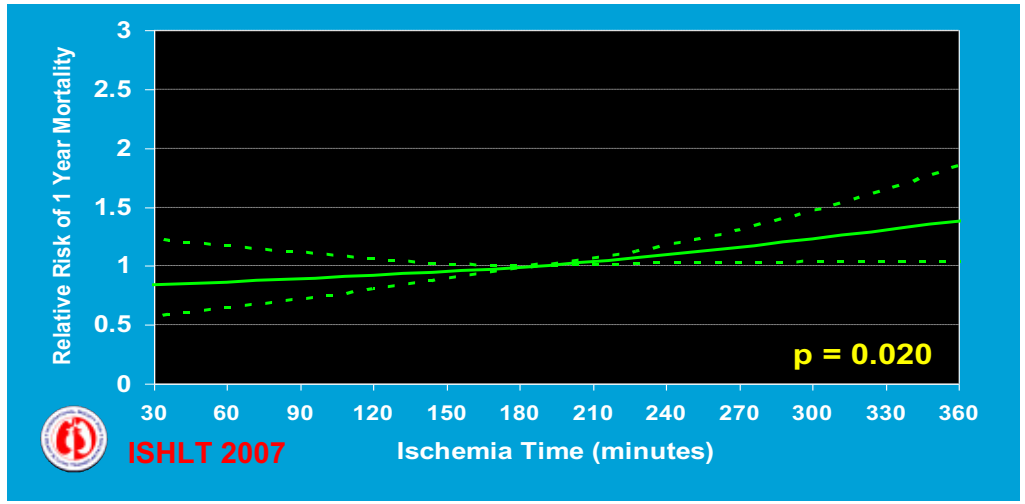

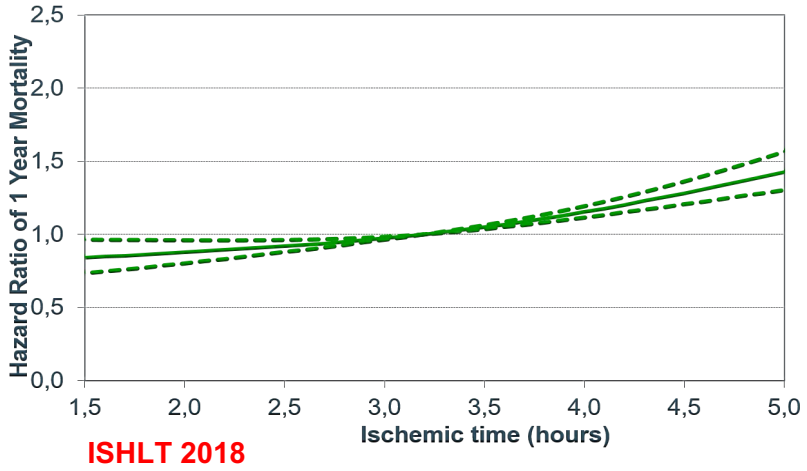

NIHP

- SCS is the standard method for organ preservation
- Limitations SCS
  - Prolonged preservation leads to tissue damage
  - Difficulty to assess donor function
  - Limited opportunity for organ repair
- Need to extend preservation times

NIHP

SCANDINAVIAN CARDIOVASCULAR JOURNAL, 2016
VOL. 50, NO. 5-6, 362–366
http://dx.doi.org/10.1080/14017431.2016.1213876

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ORIGINAL ARTICLE

Intact endothelial and contractile function of coronary artery after 8 hours of heart preservation

Guangqi Qin, Trygve Sjöberg, Qiuming Liao, Xiaoke Sun and Stig Steen

Department of Cardiothoracic Surgery, Lund University, and Skåne University Hospital, Lund, Sweden

ABSTRACT

Objectives. The aim of the study was to investigate if adequate preservation of coronary artery endothelium-dependent relaxation and contractility may be obtained after 8 hours of non-ischemic heart preservation. *Design.* Porcine hearts were perfused for 8 hours at 8 °C, either in cycles of 15 minutes perfusion and 60 minutes non-perfusion, or by continuous perfusion. The perfusate consisted of a cardioplegic, hyperoncotic nutrition solution with oxygenated red cells, and the perfusion pressure was 20 mmHg. In organ baths, coronary artery segments from the preserved hearts were studied and compared to fresh controls. *Results.* Endothelium-dependent relaxation and contractility were fully preserved after both intermittent and continuous perfusion, as compared to fresh controls. No myocardial edema was seen; water content of the myocardium was 79.5 ± 0.2%, 79.0 ± 0.4% and 79.0 ± 0.3% (ns) for fresh controls, intermittently perfused, and continuously perfused hearts, respectively. *Conclusion.* Intact endothelial and contractile function of coronary artery may be obtained after 8 hours of non-ischemic heart preservation.

ARTICLE HISTORY
Received 19 May 2016
Revised 28 June 2016
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Published online 2 August 2016

KEYWORDS
Heart preservation; coronary contractility; coronary endothelial function

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2020, VOL. 54, NO. 1, 59–65
https://doi.org/10.1080/14017431.2019.1684553

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ORIGINAL ARTICLE

OPEN ACCESS Check for updates

Intact coronary and myocardial functions after 24 hours of non-ischemic heart preservation

Guangqi Qin, Björn Wohlfart, Long Zuo, Jingfeng Hu, Trygve Sjöberg and Stig Steen

Department of Cardiothoracic Surgery, Lund University and Skåne University Hospital, Lund, Sweden

ABSTRACT

Objectives. The aim of this study was to investigate endothelium dependent relaxation (EDR) in coronary artery and the myocardial contractility after 24 h of non-ischemic heart preservation (NIHP). *Design.* Explanted cardioplegic hearts from six pigs were preserved by NIHP for 24 h. The perfusion medium consisted of an albumin containing hyperoncotic cardioplegic nutrition-hormone solution with erythrocytes to a hematocrit of 10%. Coronary artery ring segments were then studied in organ baths. Thromboxane A_2 was used for vasocontraction and Substance P to elicit endothelium dependent relaxation. A heart trabecula from the right ventricle was mounted in an organ bath and a special stimulation protocol was used to characterize myocardial contractility. Fresh cardioplegic hearts from 11 pigs were used as controls. The water content of the hearts was calculated. *Results.* There was no significant difference between NIHP and fresh controls regarding EDR (91.2 ± 1.2% vs 93.1 ± 1.8%). The contraction force, potentiation and calcium recirculation fraction did not differ between the groups. The water content of the myocardium was 79.3 ± 0.2% for NIHP and 79.5 ± 0.2% for controls. *Conclusions.* NIHP for 24 h keeps coronary artery EDR and myocardial contractility intact and causes no edema.

ARTICLE HISTORY
Received 28 January 2019
Revised 20 August 2019
Accepted 18 October 2019

KEYWORDS
Non-ischemic; heart preservation; myocardial contractility; endothelium dependent relaxation

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http://dx.doi.org/10.3109/14017431.2016.1154598

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ORIGINAL ARTICLE

OPEN ACCESS

Safe orthotopic transplantation of hearts harvested 24 hours after brain death and preserved for 24 hours

Stig Steen[a], Audrius Paskevicius[a], Qiuming Liao[a] and Trygve Sjöberg[a]

Department of Cardiothoracic Surgery, Skåne University Hospital, and Lund University,, Lund, Sweden

UZ LEUVEN

NIHP

ARTICLE

https://doi.org/10.1038/s41467-020-16782-9 OPEN

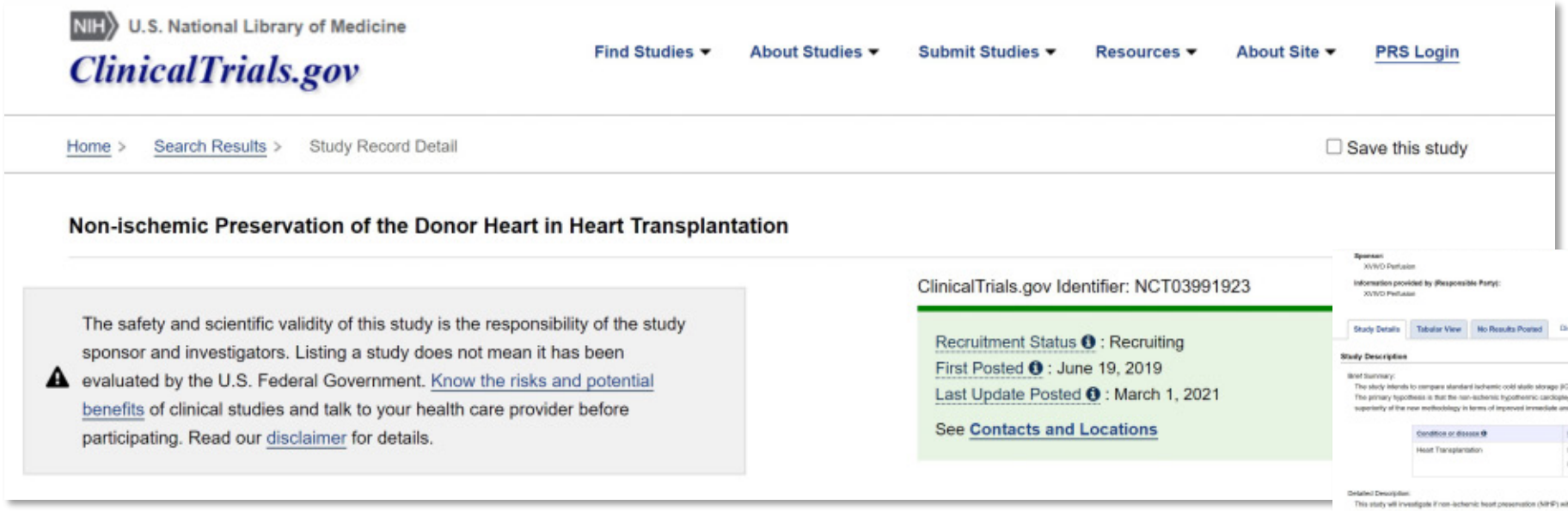
Check for updates

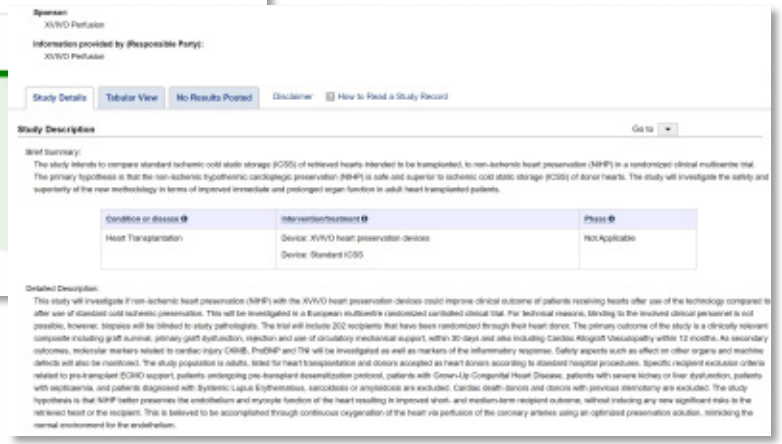
A nonrandomized open-label phase 2 trial of nonischemic heart preservation for human heart transplantation

Johan Nilsson[1✉], Victoria Jernryd[1], Guangqi Qin[1], Audrius Paskevicius[1], Carsten Metzsch[1], Trygve Sjöberg[1] & Stig Steen[1]

UZ LEUVEN

NIHP – EU Trial





Leuven – NIHP

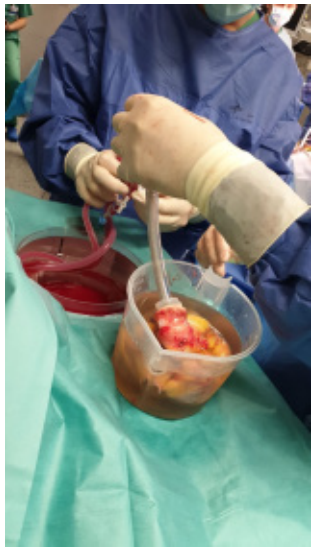
Milestones overview

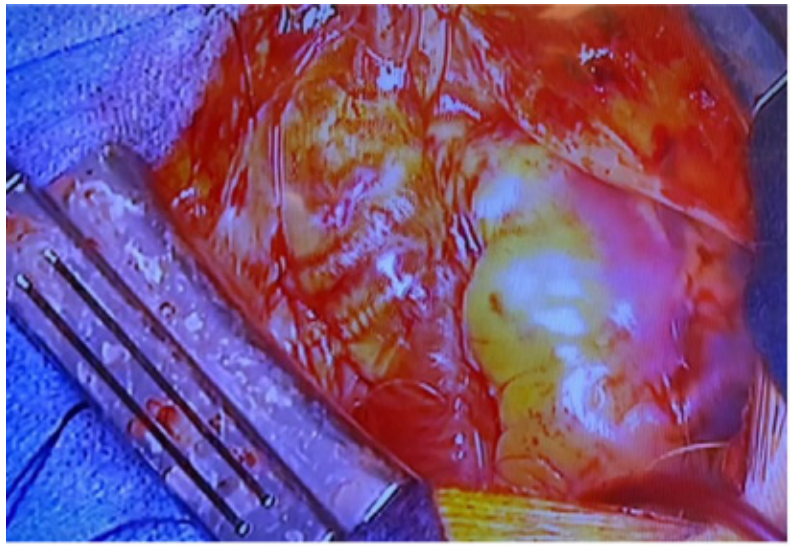
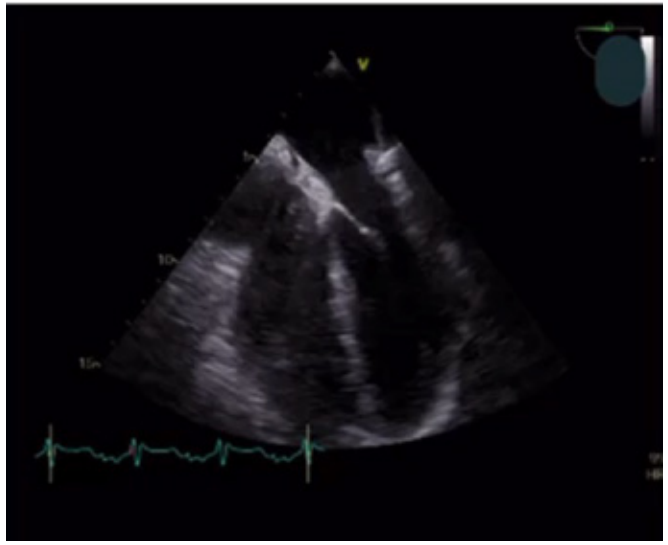
- June 6, 2019 - XVIVO NIHP File received by the UZL Clinical Trial Center
- January 2020 – Training nursing, perfusion, residents & staff
- March 24, 2020 – Approval by the Ethical Committee
- April 2020 – Site initiation visit, CRF, …
- June 17, 2020 – Contract XVIVO/LRD signed
- June 20, 2020 – First IC signed
- November 25, 2020 – Patient 1001 HTx– Patient randomized to NIHP

Leuven – NIHP

Milestones overview

- November 25, 2020 – Patient 1001 HTx

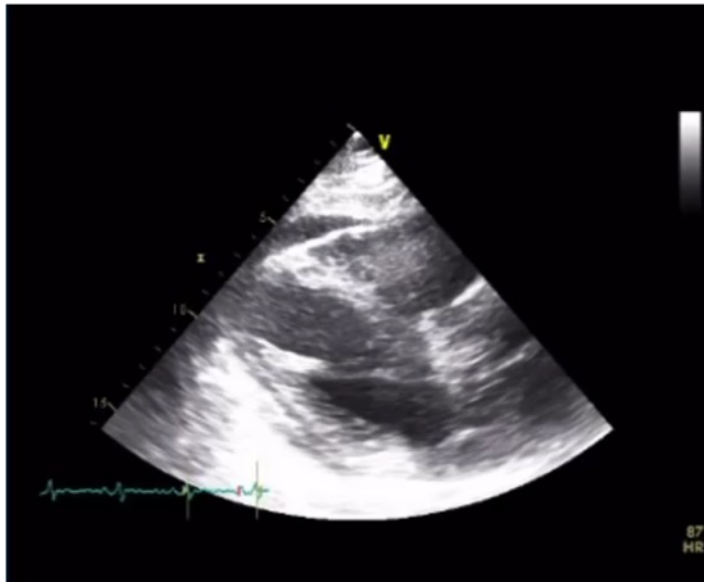


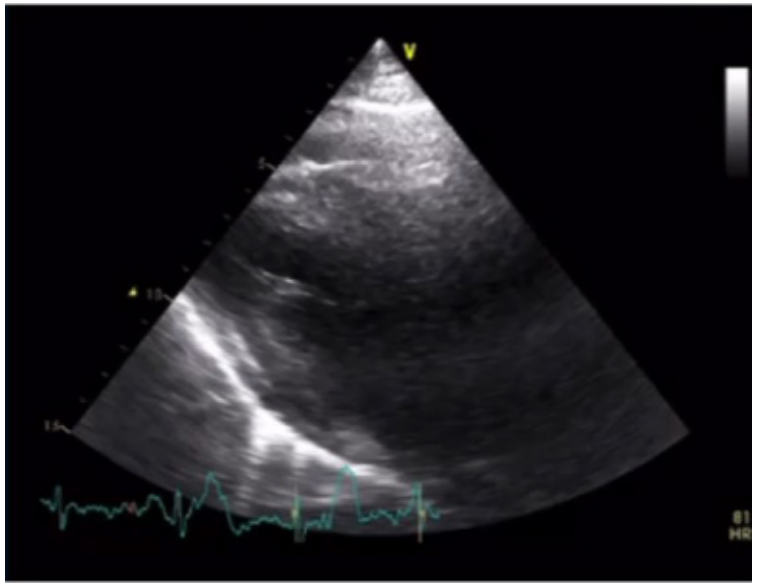



Leuven – NIHP

Milestones overview

- November 25, 2020 – Patient 1001 HTx





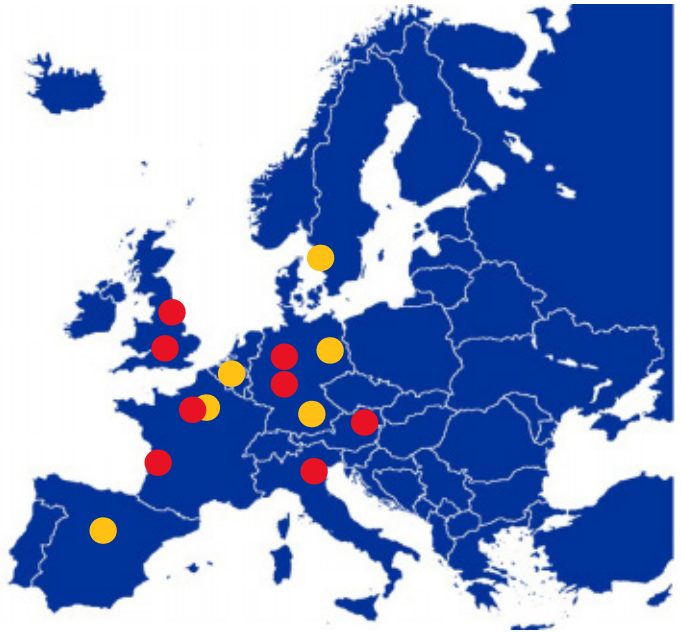
Leuven – NIHP

Milestones overview

- Since June 15th, 14 patients randomized
  - 6 Randomized to NIHP, All transplanted
  - 7 Randomized to Control
  - 1 Donor VSD closure – recipient succesfully transplanted
  - 3 Re-Htx, 3 DCD, 1 Cong
  - 1 patient transplanted while considering IC

NIHP – EU Trial

- Coordinating Principal Investigator Prof Rega, Leuven
- Randomized trial (202 pt)
  Ice vs. NIHP
- 6 active sites
  Leuven, Paris, Gothenburg, Madrid, Berlin, Munich.
- Additional site under preparation
- First patient reported Dec 2020
- Currently about 40 patient included



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Potential Benefits – Short term

Xvivo Heart was again terrific – even with severe PH in recipient no real problems

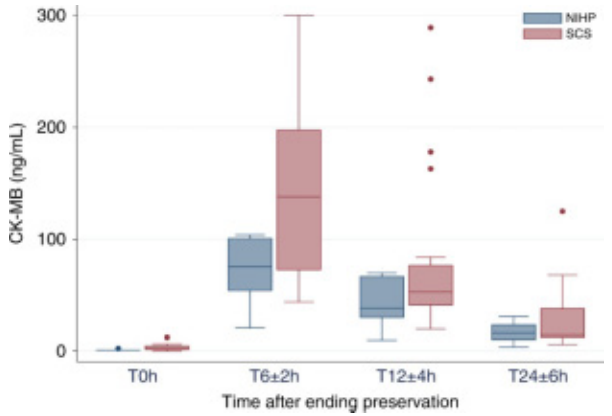
(also thanks to top anesthesia off course)

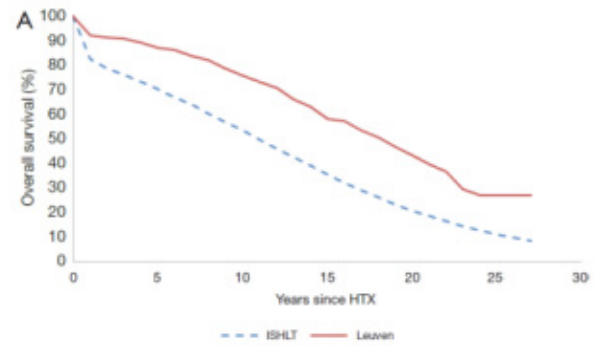
Potential Benefits – Long term

- Graft outcome
- Logistics
- Organ recovery marginal donors
- DPP in DCD heart transplantation

Potential Benefits – Long term

- Graft outcome
  - Outcome after heart tx
  - LVAD so far no major advancement
- Logistics
  - Paper 24 hrs
- Organ recovery marginal donors
- DPP in DCD heart transplantation





Potential Benefits – Long term

- Graft outcome
- Logistics

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VOL. 50, NO. 3, 193–200
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ORIGINAL ARTICLE

OPEN ACCESS

Safe orthotopic transplantation of hearts harvested 24 hours after brain death and preserved for 24 hours

Stig Steen[a], Audrius Paskevicius[a], Qiuming Liao[a] and Trygve Sjöberg[a]

Department of Cardiothoracic Surgery, Skåne University Hospital, and Lund University,, Lund, Sweden

- Organ recovery marginal donors
- DPP in DCD heart transplantation

UZ LEUVEN

Potential Benefits – Long term

- Graft outcome
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Non-Ischemic Heart Preservation

Capital Markets Day

November 23, 2021

Filip Rega, MD, PhD

Head of Clinic, University Hospitals Leuven, Belgium
Professor, Cardiovascular Sciences, KU Leuven, Belgium
Director of the Leuven Surgical Heart Transplant Program
Principal Investigator NIHP Trial

Abdominal

Arjan v.d. Plaats, R&D Director and
Johan Holmström, CCO

XVIVO

Overview: Abdominal

The market

Key facts

No of transplants*
- Kidney 62,000**
- Liver 28,000

Organ utilization rate
- Kidney 67%
- Liver 65%

Active clinics
- Kidney 2,200
- Liver 1,000

Main market challenges
- Growing need for transplantation (incl. use of DCD)
- Varying levels of reimbursement

XVIVO today

Market presence

XVIVO products
- Liver Assist
- Kidney Assist
- Kidney Assist Transport v.1

- v.2 not yet reg. approved -

Where Abdominal supports our strategy

Strategic focus areas 2022 – 2026

- Global leader Abdominal (the US)
- Increase penetration of machine perfusion
- Secure all-inclusive reimbursement in key geographies
- China to become second largest market

*2019 figures

**Deceased donors. 98,000 including donations from living donors.

Abdominal product line

Arjan v.d. Plaats, R&D Director

XVIVO

XVIVO – Abdominal portfolio

Kidney Assist Transport

XVIVO's portable system for cold, oxygenated perfusion of donor kidneys

Liver Assist

XVIVO's platform for cold and warm oxygenated perfusion of donor livers

XVIVO's Kidney Assist Transport

- XVIVO's Kidney Assist Transport provides improved preservation of donor kidneys leading to better transplantation outcomes
- Cold machine perfusion leads to improved graft survival and reduced delayed graft function after transplantation compared to static cold storage preservation of all donor types[1,2]
- Cold OXYGENATED machine perfusion leads to even better kidney function, higher graft survival and less complications after transplantation of DCD kidneys[3]

[1] Moers C, et al. Machine Preservation Trial Study Group. Machine perfusion or cold storage in deceased-donor kidney transplantation. N Engl J Med. 2012 Feb 23;366(8):770-1.

[2] Brat A, et al. Hypothermic Machine Perfusion as a National Standard Preservation Method for Deceased Donor Kidneys. Transplantation. 2021 Jun 23

[3] Jochmanns I, et al. Oxygenated versus standard cold perfusion preservation in kidney transplantation (COMPARE): a randomised, double-blind, paired, phase 3 trial. The Lancet. November 2020;396(10263):1653-1662.

Results from the COMPARE trial[1]

- United Kingdom (Ploeg, Oxford)
- The Netherlands (Hofker, Groningen)
- Belgium (Jochmans, Leuven)

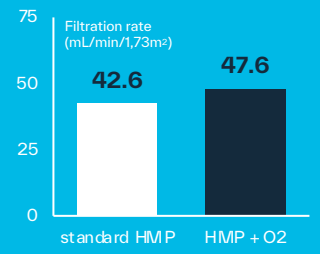
- Double blinded
- Computer- randomized study
- 106 kidney pairs included

- Donor >50 years
- Donated after Circulatory Death (DCD) III (high risk donors)
- Kidney pair was its own control group

Standard-HMP

VS.

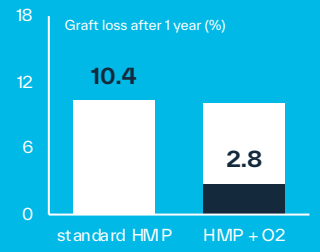
HMP+O2



Improved renal function by

11.7%

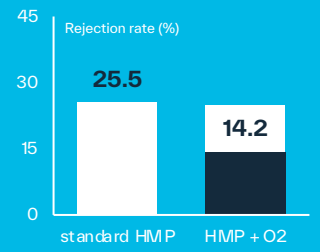
P=0.035



Reduction of graft failure by

73.1%

P=0.021



Lowered incidence of acute rejection by

44%

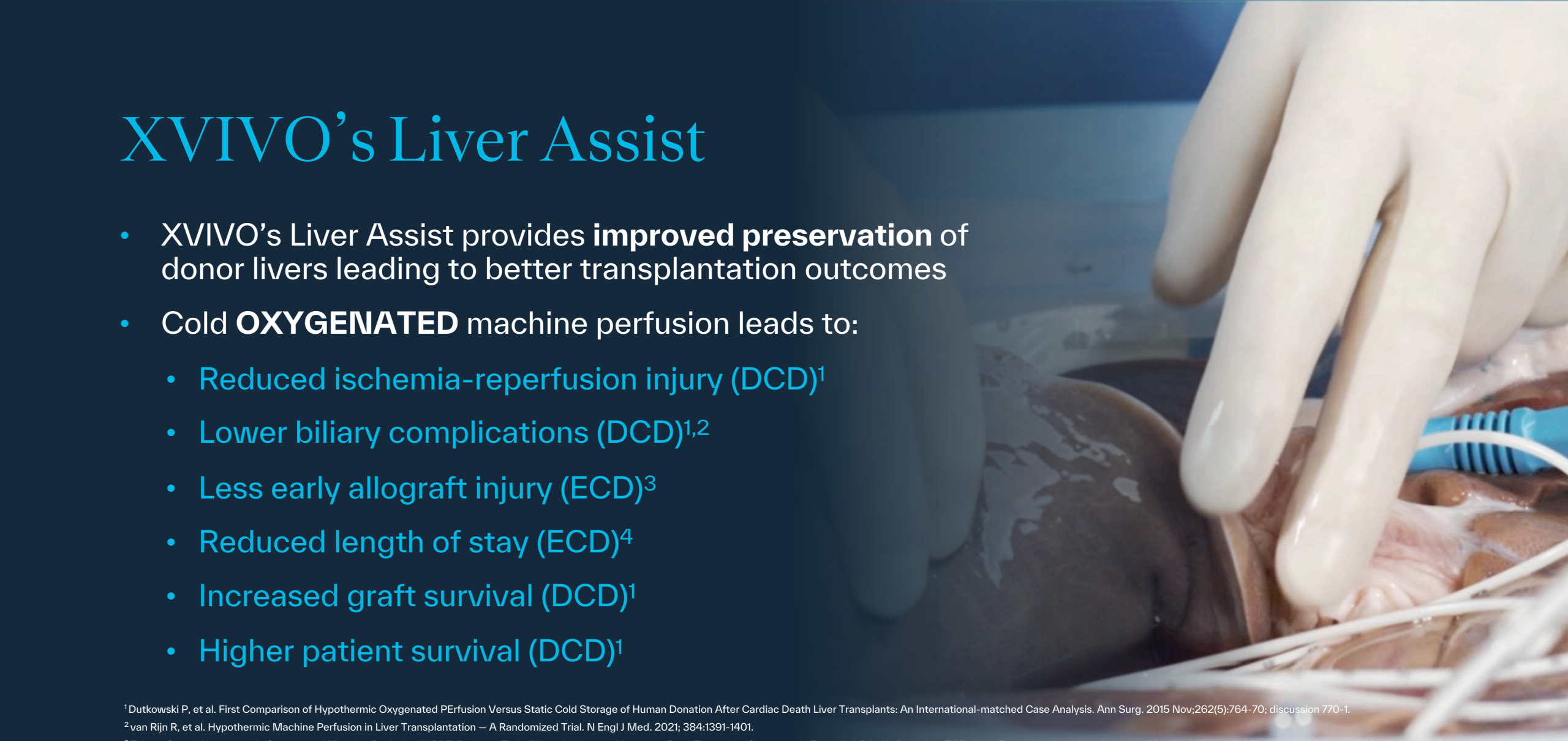
P=0.040

[1] Johmanns I, et al. Oxygenated versus standard cold perfusion preservation in kidney transplantation (COMPARE): a randomised, double-blind, paired, phase 3 trial. The Lancet. November 2020;396(10263):1653-1662.

XVIVO

XVIVO's Liver Assist

- XVIVO's Liver Assist provides **improved preservation** of donor livers leading to better transplantation outcomes
- Cold **OXYGENATED** machine perfusion leads to:
  - Reduced ischemia-reperfusion injury (DCD)[1]
  - Lower biliary complications (DCD)[1,2]
  - Less early allograft injury (ECD)[3]
  - Reduced length of stay (ECD)[4]
  - Increased graft survival (DCD)[1]
  - Higher patient survival (DCD)[1]



[1] Dutkowski P, et al. First Comparison of Hypothermic Oxygenated PErfusion Versus Static Cold Storage of Human Donation After Cardiac Death Liver Transplants: An International-matched Case Analysis. Ann Surg. 2015 Nov;262(5):764-70; discussion 770-1.

[2] van Rijn R, et al. Hypothermic Machine Perfusion in Liver Transplantation — A Randomized Trial. N Engl J Med. 2021; 384:1391-1401.

[3] Zoltan, C et al. Hypothermic Oxygenated Machine Perfusion (HOPE) Reduces Early Allograft Injury and Improves Post-Transplant Outcomes in Extended Criteria Donation (ECD) Liver Transplantation from Donation After Brain Death (DBD), Annals of Surgery: 2021 Jul.

[4] Rayar M, et al. Hypothermic Oxygenated Perfusion Improves Extended Criteria Donor Liver Graft Function and Reduces Duration of Hospitalization Without Extra Cost: The PERPHO Study. Liver Transpl. 2021 Feb;27(3):349-362.

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Results from the dHOPE trial[1]

- The Netherlands (Porte, Groningen)
- Belgium (Monbaliu, Leuven)
- United Kingdom (Heaton, London)

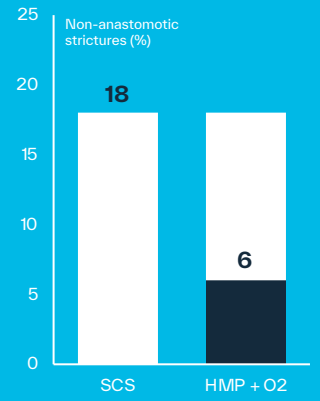
- Computer- randomized study
- 156 livers included in total

- Donated after Circulatory Death (DCD) III (high risk donors)
- Static cold storage followed by HMP+O2 or no HMP

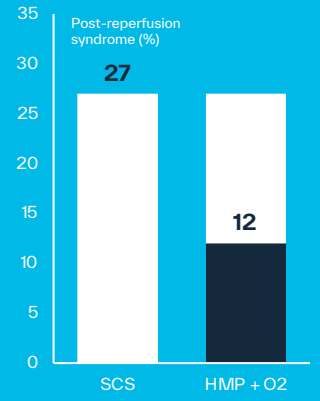
Static cold storage

VS.

Static cold storage
+
HMP+O2



67%
Lower incidence of biliary strictures



Less Post-reperfusion syndrome

56%

[1] van Rijn R, et al. Hypothermic Machine Perfusion in Liver Transplantation – A Randomized Trial. N Engl J Med. 2021; 384:1391-1401.

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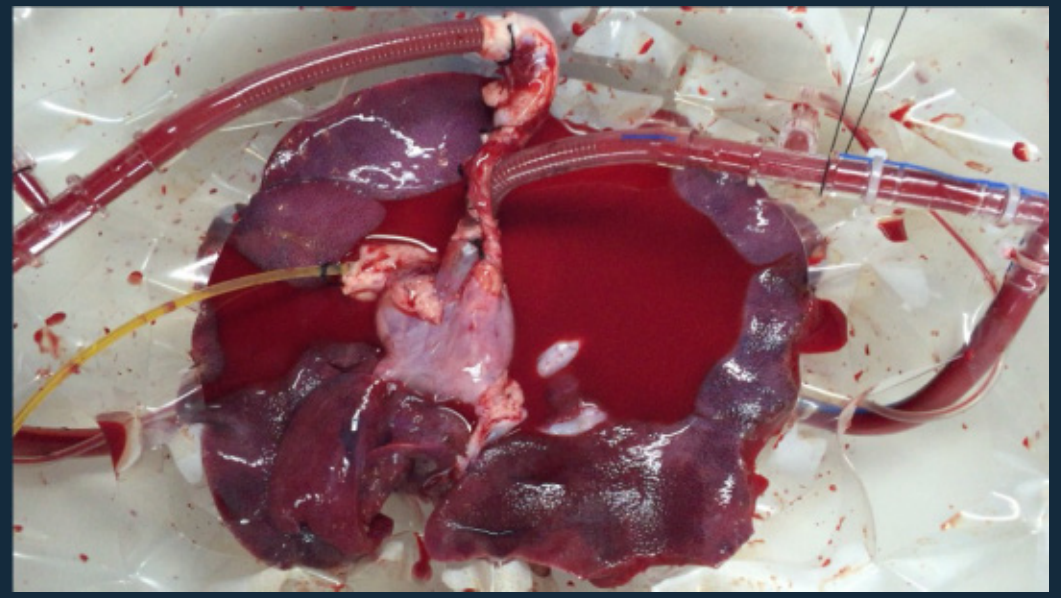
XVIVO's Liver Assist

- XVIVO's Liver Assist provides normothermic evaluation of previously-declined donor livers leading to **more livers to become available** for transplantation
  - 20% increase in liver transplantation combining hypothermic and normothermic machine perfusion[1]
  - Safe use of initially rejected donated livers[1,2]

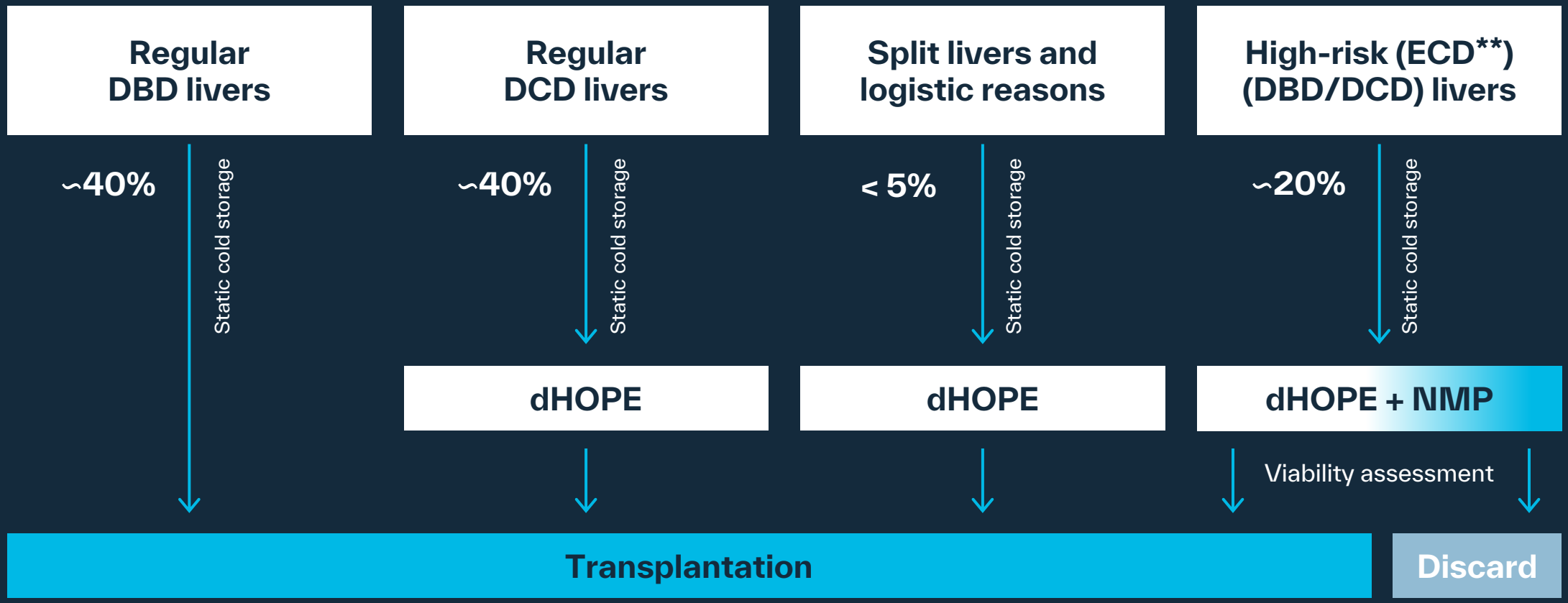


[1] van Leeuwen OB, et al. Transplantation of High-risk Donor Livers After Ex Situ Resuscitation and Assessment Using Combined Hypo- and Normothermic Machine Perfusion: A Prospective Clinical Trial. Ann Surg. 2019 Nov;270(5):906-914.

[2] Mergental H, et al. Transplantation of Declined Liver Allografts Following Normothermic Ex-Situ Evaluation. Am J Transplant. 2016 Nov;16(11):3235-3245.

XVIVO

Dedicated protocols for optimal use of donor livers



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Key take-aways: Abdominal (product line)

- Cold oxygenated machine perfusion improves success rate of kidney and liver transplantation (incl. DCD organs)
- Clinical data, from successful machine perfusion studies, has been published for kidney and liver perfusion in The Lancet and New England Journal of Medicine
- Warm perfusion of livers can increase the usage of donor livers

Abdominal – US go to market

Johan Holmström, CCO

The transplant market today*

	Liver	Kidney
No of Tx	**28,000**	**62,000**
Americas	30%	34%
Europe	32%	32%
RoW	38%	34%
Active clinics	1,000	2,200

*Solid organs from deceased donors, 2019 figures

XVIVO

US market development - Kidney and Liver

	DCD CAGR (2019-2026)	DBD CAGR (2019-2026)
Kidney	14.3%	3.2%
Liver	17.3%	2.4%

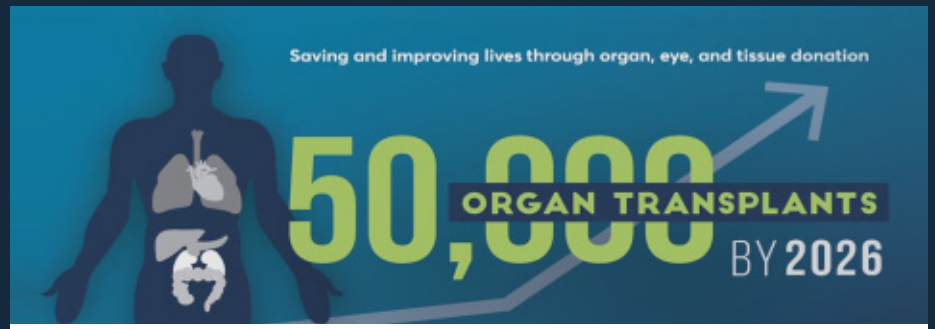
Market opportunity

- US transplants expected to increase to 50,000 by 2026
- Transplant volume development driven by disproportional growth of DCD
- XVIVO machine perfusion technology enables improved preservation of DCD organs
- YTD 2021, there is 15% increase in Kidney Tx resp 8% in Liver Tx

AOPO 50k transplants by 2026 campaign

The Association of Organ Procurement Organizations (AOPO) commits to achieving 50,000 annual transplants by 2026. AOPO and its members will work with key stakeholders to implement a series of initiatives:

1. Expand Collaboration
2. Reduce Health Inequities
3. Maximize Organ Utilization
4. Drive Innovation



AOPO
ASSOCIATION OF ORGAN PROCUREMENT ORGANIZATIONS
Saving and improving lives through organ, eye, and tissue donation

XVIVO

Launch focus – Kidney Assist Transport

- Our first product launch in the US will be Kidney Assist Transport
- The Kidney Assist Transport is XVIVO's transportable organ preservation system designed for kidneys
- In May 2021, XVIVO announced its submission of a **510(k)** file with US FDA for **Kidney Assist Transport**
- **Q3 Launch planning phase**
- The goal is to receive market clearance in the US Q4 2021

Go to market model and value proposition

- Positioned as a premium product – based on a clinical and a performance proposition
- Our clinical proposition *with quantified clinical advantages* – driving improved transplantation outcomes
- Kidney Assist Transport will accommodate customers need to improve compliance with increased performance metrics set by CMS and UNOS
- Variable go to market model of machine placements and direct sales to accelerate build of installed base and to accommodate variable customer needs
- Dedicated commercial team for Abdominal – *clinical expertise and Key Account Management*
- "Pull and Push" strategy - transplant centres and OPOs

Target launch dates – the US

Kidney Assist Transport

- Target launch in the US, in January 2022
- Selective pre-launch in Q4 2021

Liver Assist

- Process for FDA application has started

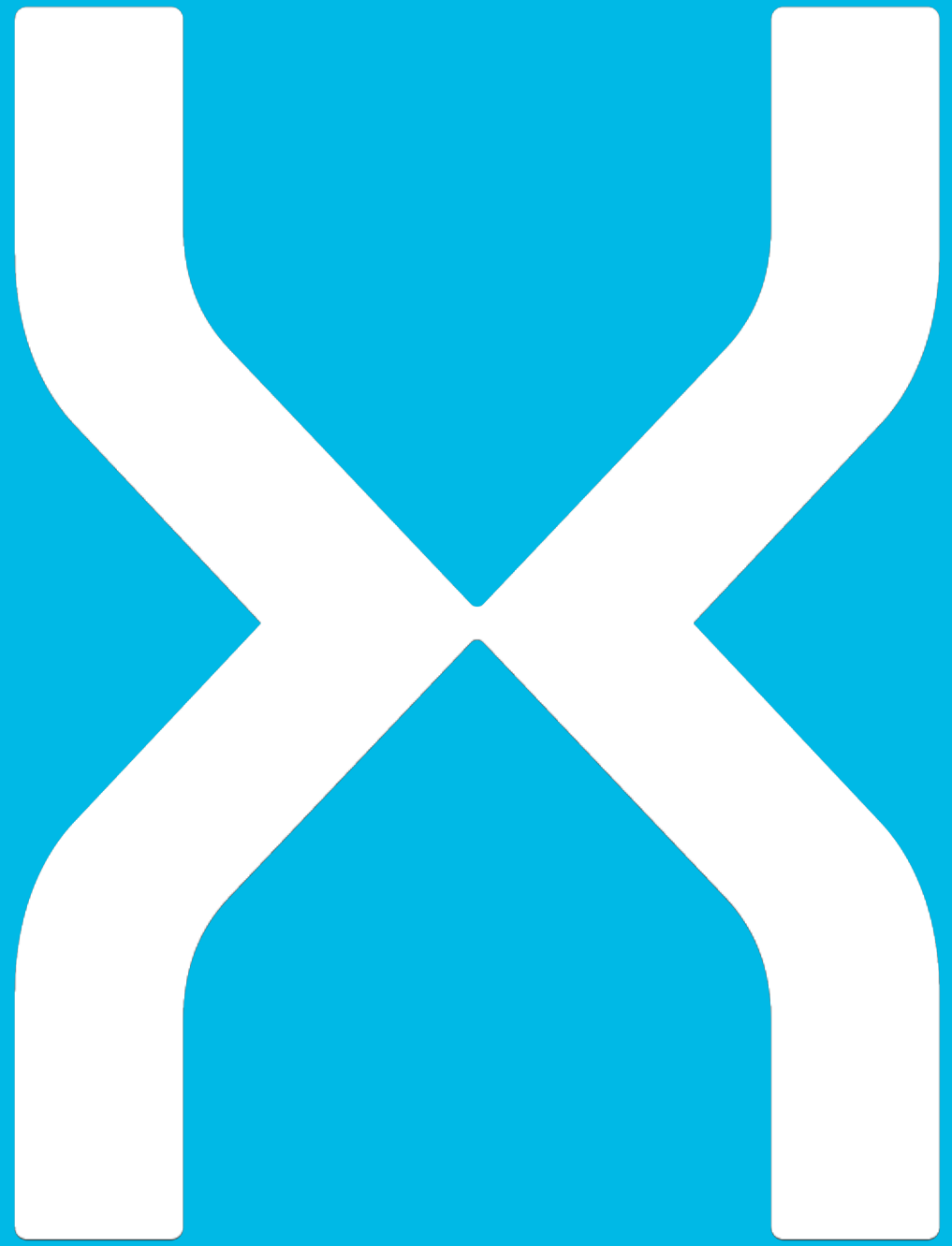
XVIVO

Key take-aways: Abdominal (US go to market)

- There is a clear ambition to significantly increase the number of transplants in the US (50k transplants in 2026)
- DCD organs will drive the increase in number of organs donated
- XVIVO's ground breaking Kidney Assist Transport device to be launched later this year, subject to 510(k) clearence
- 2022 will focus on kidney launch and liver will follow once regulatory approval given

Q&A

Break



Agenda

13.00	- 13.05	Introduction	Lars Frick, Moderator and Dag Andersson, CEO
13.05	- 13.20	Market & trends	Dag Andersson, CEO
13.20	- 13.35	Strategy	Dag Andersson, CEO and Kristoffer Nordström, CFO
13.35	- 13.50	Health economics	Johan Holmström, CCO
13.50	14.05	Q&A	
14.05	- 14.20	Break	
14.20	- 14.50	Heart	Andreas Wallinder, CMO and Professor Filip Rega, Cardiac surgeon at UZ Leuven
14.50	- 15.20	Abdominal	Arjan v.d. Plaats, R&D Director and Johan Holmström, CCO
15.20	15.35	Q&A	
15.35	- 15.50	Break	
15.50	- 16.20	Lung	Rodney Jones, Sales Director North America and Brandi Zofkie, Director at Lung BioEngineering
16.20	- 16.40	Future of transplantation	Christoffer Rosenblad, COO and Professor Muhammad M. Mohiuddin, Director Cardiac Xenotransplantation Program at University of Maryland
16.40	- 16.55	Q&A	
16.55	- 17.00	Thank You	Dag Andersson, CEO

Lung

Rodney Jones, Sales Director North America

Overview: Lung

The market

Key facts

No of transplants*
- 6,700

Organ utilization rate
- 20%

Active clinics
- 250

Main market challenges
- Growing need for transplantation (incl. < use of DCD)
- Varying levels of reimbursement

XVIVO today

Market presence

XVIVO products
- PERFADEX® Plus
- XPS™ and STEEN Solution™

- Approved in all major markets -

Where Lung supports our strategy

Strategic focus areas 2022 – 2026

- Increase penetration of machine perfusion
- Secure all-inclusive reimbursement in key geographies
- China to become second largest market

*2019 figures

Trends and innovation – the US

Rodney Jones, Sales Director North America

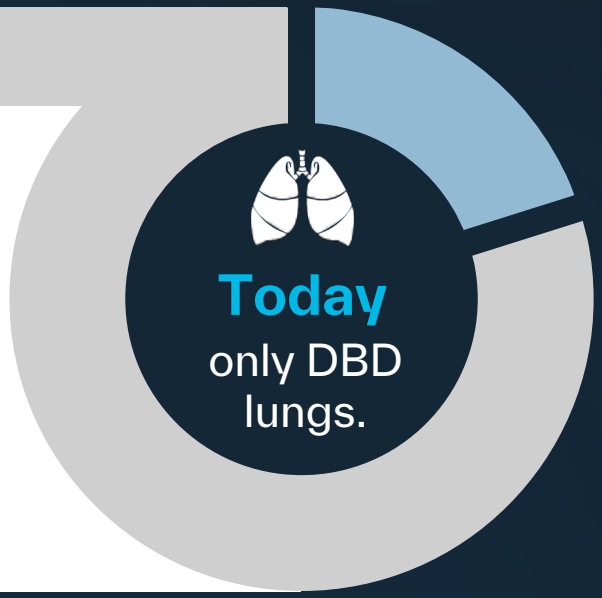
Doubling the number of available lungs

Cold preservation

enables use of approx.

20%

of all donated standard DBD lungs.



PROCUREMENT → COLD PRESERVATION → TRANSPLANTATION

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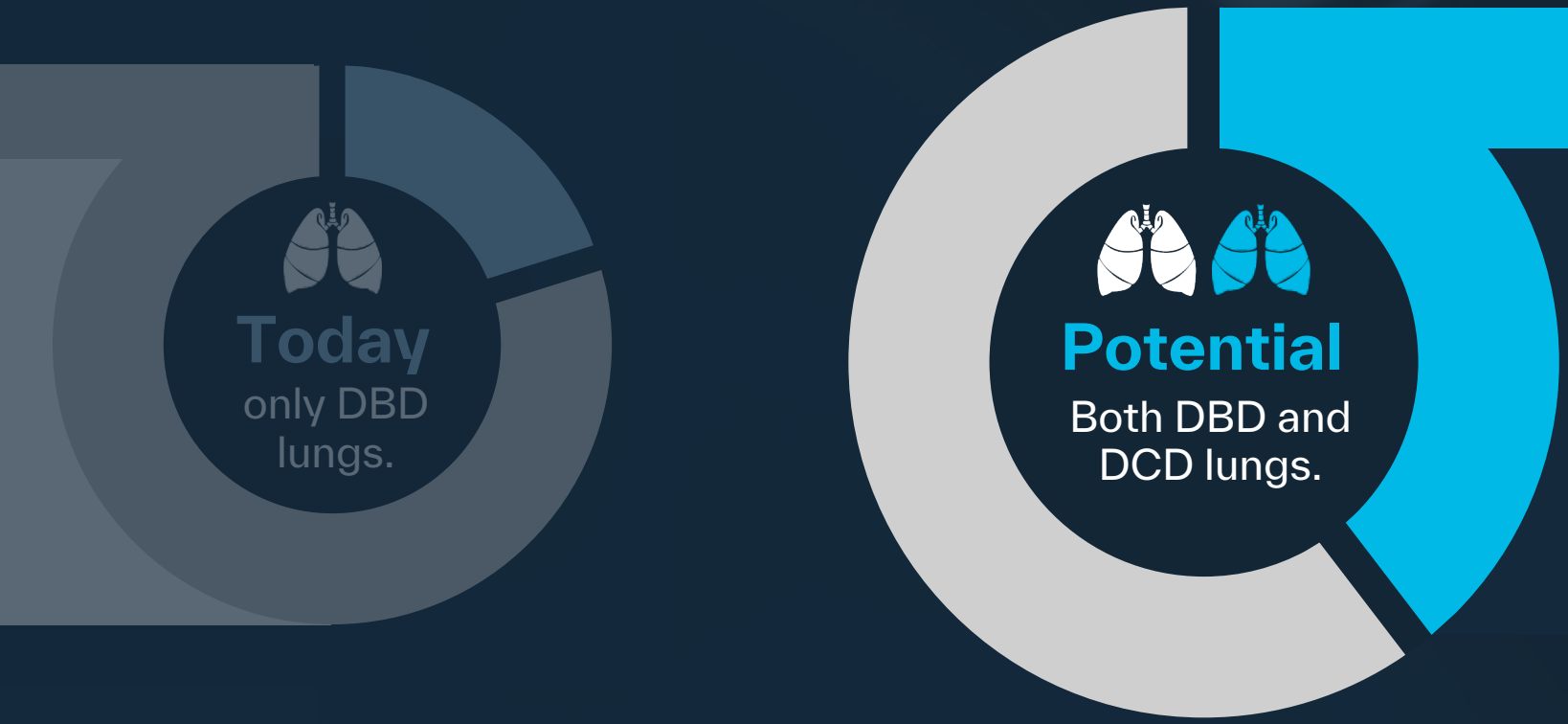
Doubling the number of available lungs



Cold + Warm preservation

enables use of approx.

40%

of all donated standard DBD and DCD lungs.

PROCUREMENT → COLD PRESERVATION → EVALUATION OF LUNG THROUGH EVLP → TRANSPLANTATION

XVIVO

Our EVLP Platform

XPS™ with STEEN Solution™

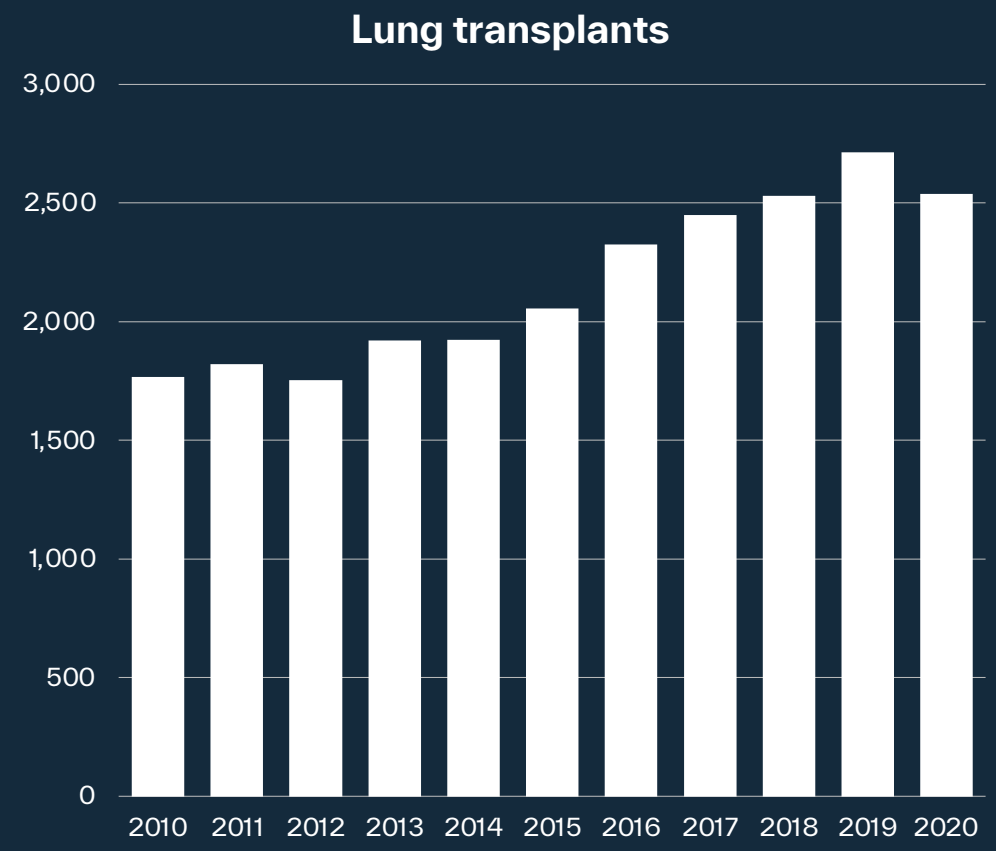
A fully integrated platform for normothermic EVLP

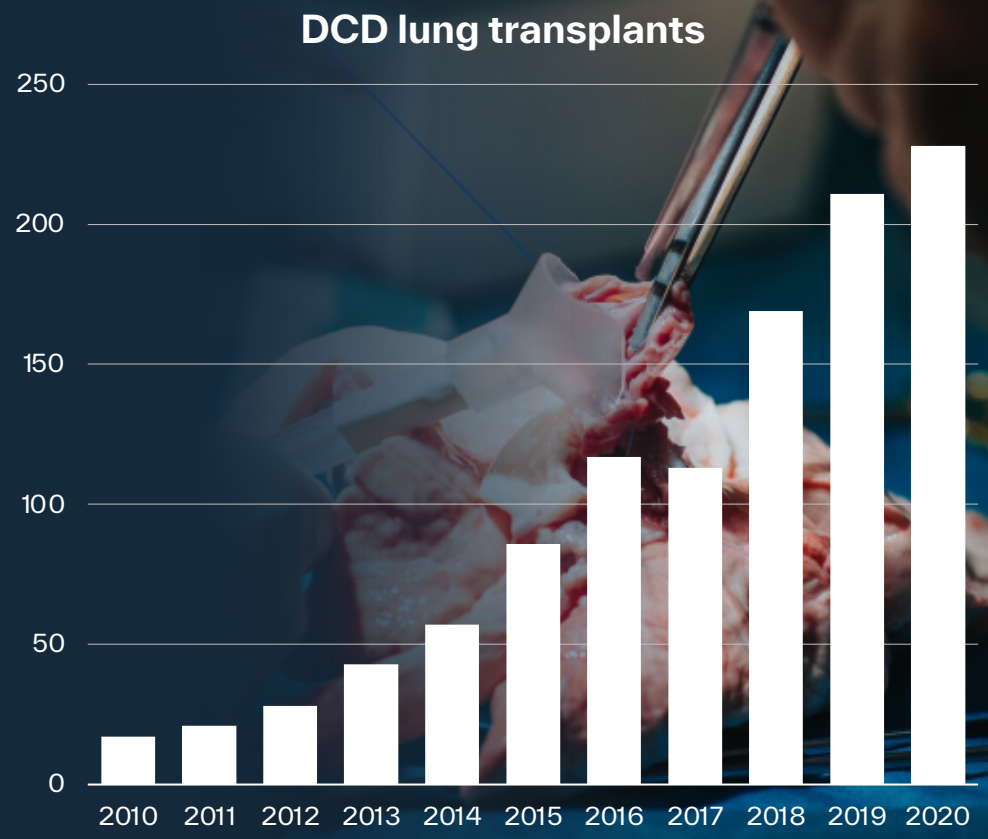
EVLP

Expanding the available donor pool

The ultimate objective of EVLP is to **expand the available donor pool** and **minimize mortality and morbidity** on the transplant waiting list.

Trends in lung transplants





OPTN data through December 31st, 2020

Exploring NOVEL technique for expanding donor pool

5 Transplants 2.5 WIT

Zero PGD3 72hrs

30 day mortality zero

80% 1 yr survival

Am J Transplant. 2020 Jun;20(6):1574-1581. doi: 10.1111/ajt.15795. Epub 2020 Feb 29.

Initial lung transplantation experience with uncontrolled donation after cardiac death in North America

Andrew Healey [1 2 3], Yui Watanabe [4], Caitlin Mills [1], Michele Stoncius [1], Susan Lavery [1], Karen Johnson [1], Robert Sanderson [1], Atul Humar [4], Jonathan Yeung [4], Laura Donahoe [4], Andrew Pierre [4], Marc de Perrot [4], Kazuhiro Yasufuku [4], Thomas K Waddell [4], Shaf Keshavjee [4], Marcelo Cypel [4]

Affiliations + expand

PMID: 31995660 DOI: 10.1111/ajt.15795

Free article

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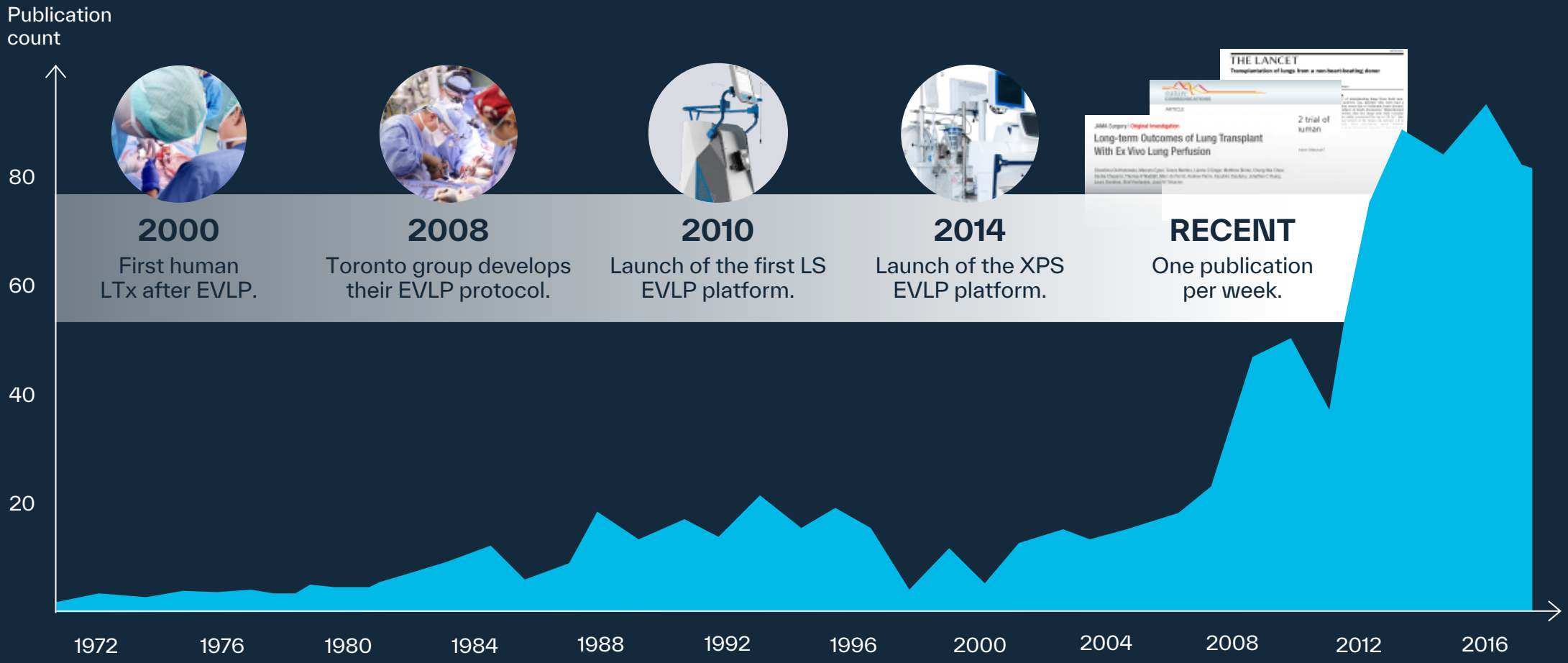
EVLP publications over time



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EVLP during pandemic

- 2016 only 1% of Lung Txp was EVLP
- 2020 25% of Lung Txp was EVLP
- 1 of 4 programs >100 Lung Txp
- Rationale for EVLP
  - Logistics
  - 3rd party recovery services
  - Marginal criteria assessment
  - Additional COVID testing

(757)

The Evolving Role of Ex Vivo Lung Perfusion during the COVID-19 Pandemic

K.S. Ayyat, T. Okamoto, I. Sakanoue, H. Elgharably, M.M. Budev, J.J. Yun and K.R. McCurry Cleveland Clinic Foundation, Cleveland, OH.

Conclusion: Maintaining LTx activity with EVLP was feasible in the early phases of the COVID-19 pandemic. EVLP enabled our team to solve challenges with donor evaluation and logistics. By enabling donor assessment after local procurement, EVLP also increased the procurement team's safety. In the future, these newer EVLP indications may be applicable beyond the COVID-19 pandemic.

In the future, these newer EVLP indications may be applicable beyond the COVID-19 pandemic.

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Preclinical drug discovery

> JCI Insight. 2018 Oct 4;3(19):e95515. doi: 10.1172/jci.insight.95515.

Ex vivo lung perfusion as a human platform for preclinical small molecule testing

Nathaniel M Weathington [1], Diana Álvarez [1 2], John Sembrat [1 2], Josiah Radder [1], Nayra Cárdenes [1 2], Kentaro Noda [3], Qiaoke Gong [1], Hesper Wong [1], Jay Kolls [4], Jonathan D'Cunha [3], Rama K Mallampalli [1 5 6], Bill B Chen [1 5], Mauricio Rojas [1 2 7]

Affiliations + expand

PMID: 30282819 PMCID: PMC6237445 DOI: 10.1172/jci.insight.95515

Free PMC article

Mallinckrodt Initiates Proof-of-Concept Study of Nitric Oxide Gas in Ex-Vivo System of Human Lung Transplants

Mallinckrodt Pharmaceuticals

-- Study Begins Evaluation on First Set of Lungs, Will Assess Organs Using Proprietary Grading System --

NEWS PROVIDED BY
Mallinckrodt plc →
Aug 01, 2018, 16:45 ET

SHARE THIS ARTICLE

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Key take-aways: Lung

- EVLP is a safe and efficatious way to increase the number of life saving lung transplants
- The pandemic has demonstrated that there are potential new indications for EVLP
- EVLP growth is trending upward and is a standard practice in high performing lung transplant centers

Lung bioengineering

- Centralized Ex Vivo Lung Perfusion

Brandi Zofkie, Director Lung Bioengineering

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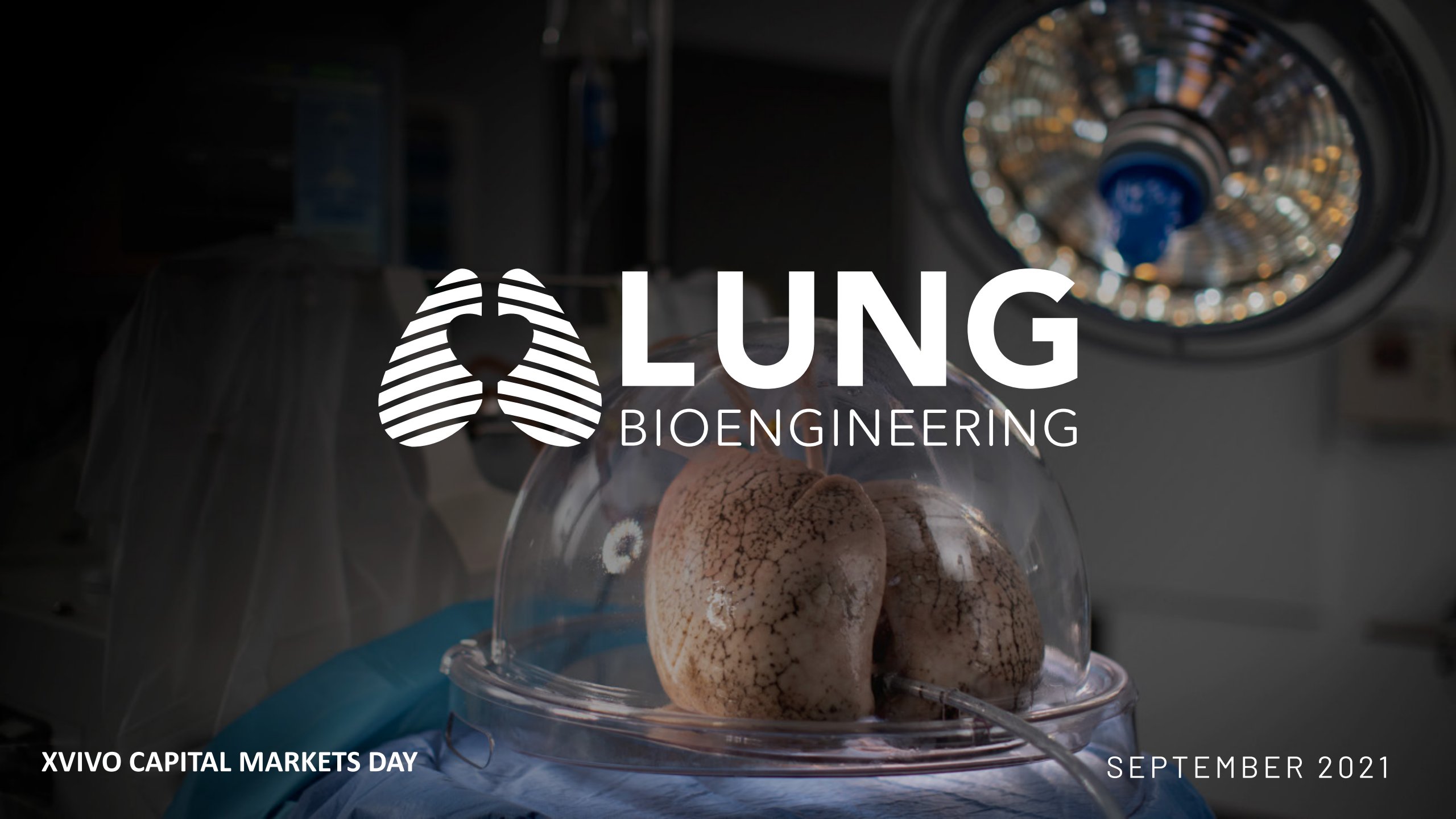


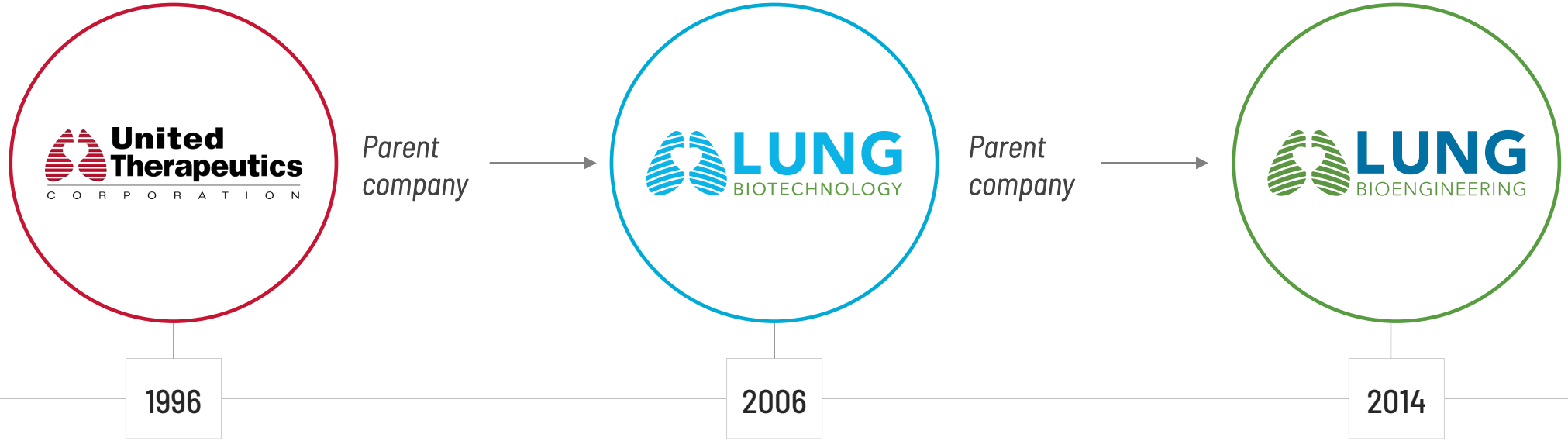
LUNG BIOENGINEERING

XVIVO CAPITAL MARKETS DAY

SEPTEMBER 2021

Our Story

WHO WE ARE

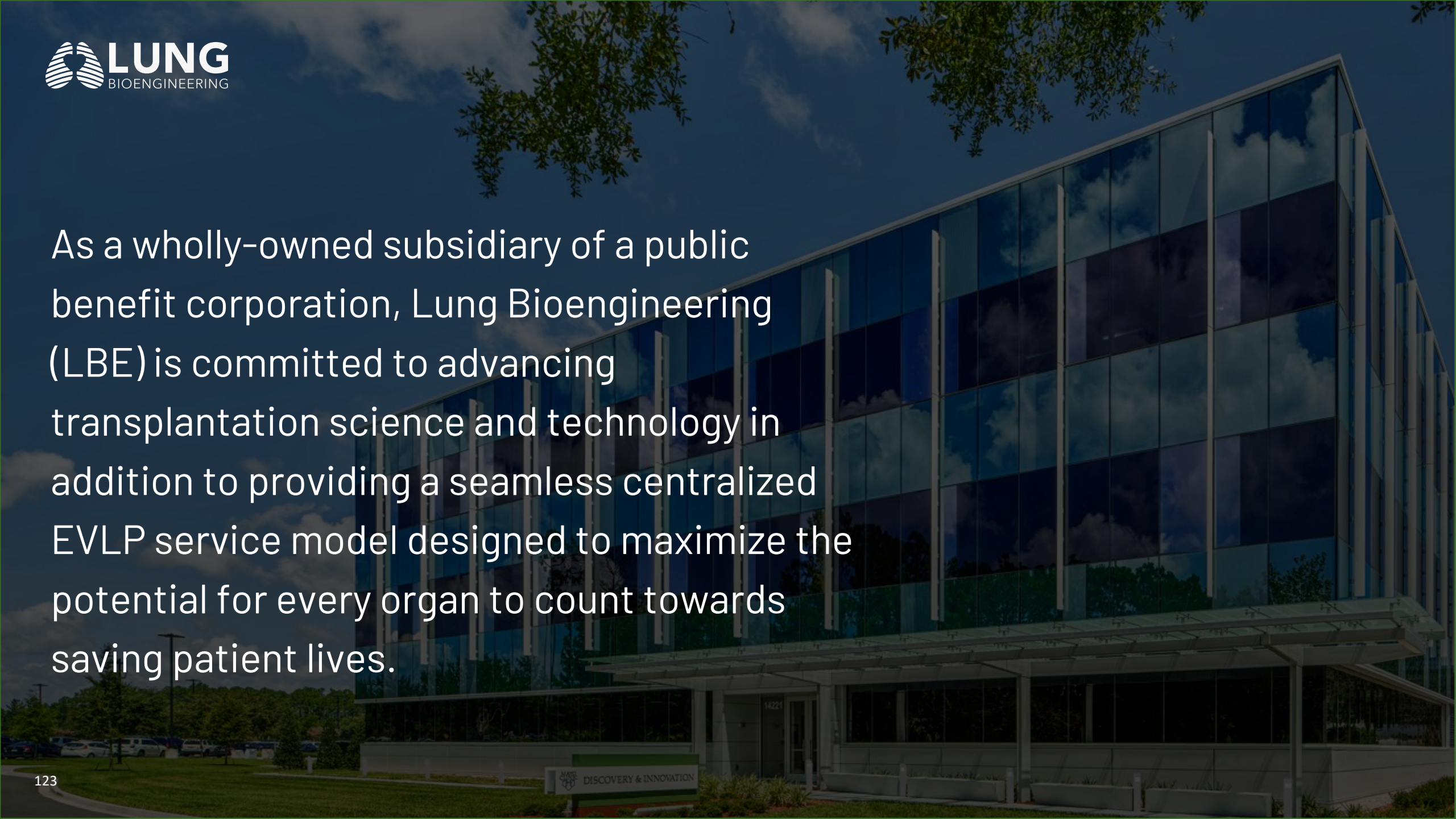


United Therapeutics Corporation was founded in 1996 by Martine Rothblatt following the diagnosis of her daughter with pulmonary arterial hypertension (PAH). A biotech company born out of exceptional circumstances, United Therapeutics develops unique products for chronic and life-threatening cardiovascular diseases as well as cancer.

Under the name of Lung Rx, **Lung Biotechnology** was established in 2006 as part of United Therapeutics' work to address the acute national shortage of transplantable lungs and other organs with a variety of technologies that either delay the need for such organs or expand the supply. Lung Biotechnology is the first public benefit corporation subsidiary of a public biotechnology or pharmaceutical company.

Founded in 2014, **Lung Bioengineering Inc.** is a wholly-owned subsidiary of Lung Biotechnology PBC. Our mission is to be the most trusted provider of centralized organ services, delivering a seamless customer experience and supporting innovative research in order to expand the supply of transplantable organs. In September 2021, the 191st patient was transplanted from EVLP, a figure that reflects our growing impact in the transplant field.

The EVLP service described in this presentation is for the United States only.



As a wholly-owned subsidiary of a public benefit corporation, Lung Bioengineering (LBE) is committed to advancing transplantation science and technology in addition to providing a seamless centralized EVLP service model designed to maximize the potential for every organ to count towards saving patient lives.

Challenges in Transplantation

WHAT WE DO

THE PROBLEM

LOGISTICAL CHALLENGES AND INADEQUATE INFORMATION

The current process that precedes the acceptance of a lung for transplant is complex.

Due to logistical challenges and incomplete information, transplant surgeons are often forced to make time-critical decisions under conditions that are not ideal.

THE ANSWER

REMOVING BARRIERS AND PROVIDING TOUCHPOINTS THROUGHOUT THE ENTIRE PROCESS

Lung Bioengineering's unique centralized Ex Vivo Lung Perfusion (EVLP) service is the first of its kind.

We use FDA-approved XVIVO Perfusion System (XPS™) technology and provide centers with the tools required to make more informed decisions and improve patients' chances of receiving a lung transplant. Our model is also designed to remove some of the resource burden experienced by transplant centers.

What is a Centralized EVLP Service?

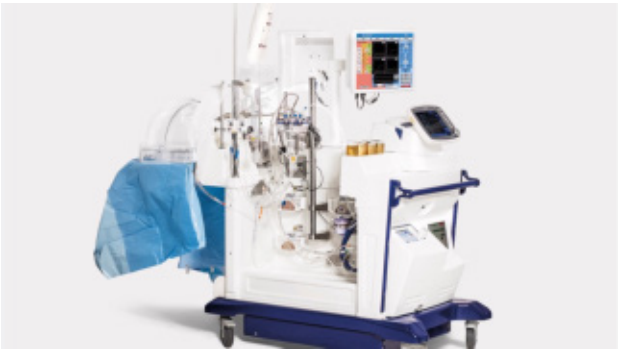
WHAT WE DO

Lung Bioengineering's centralized EVLP service model supports transplant centers by removing barriers and providing touchpoints at every step of the donation and transplantation process in order to optimize organ utilization.

We offer a seamless customer experience for the FDA approved XPS ™ EVLP technology to deliver an unrivalled solution for EVLP services and logistics.

FIRST OF ITS KIND FACILITIES

TEAM OF EXCELLENCE

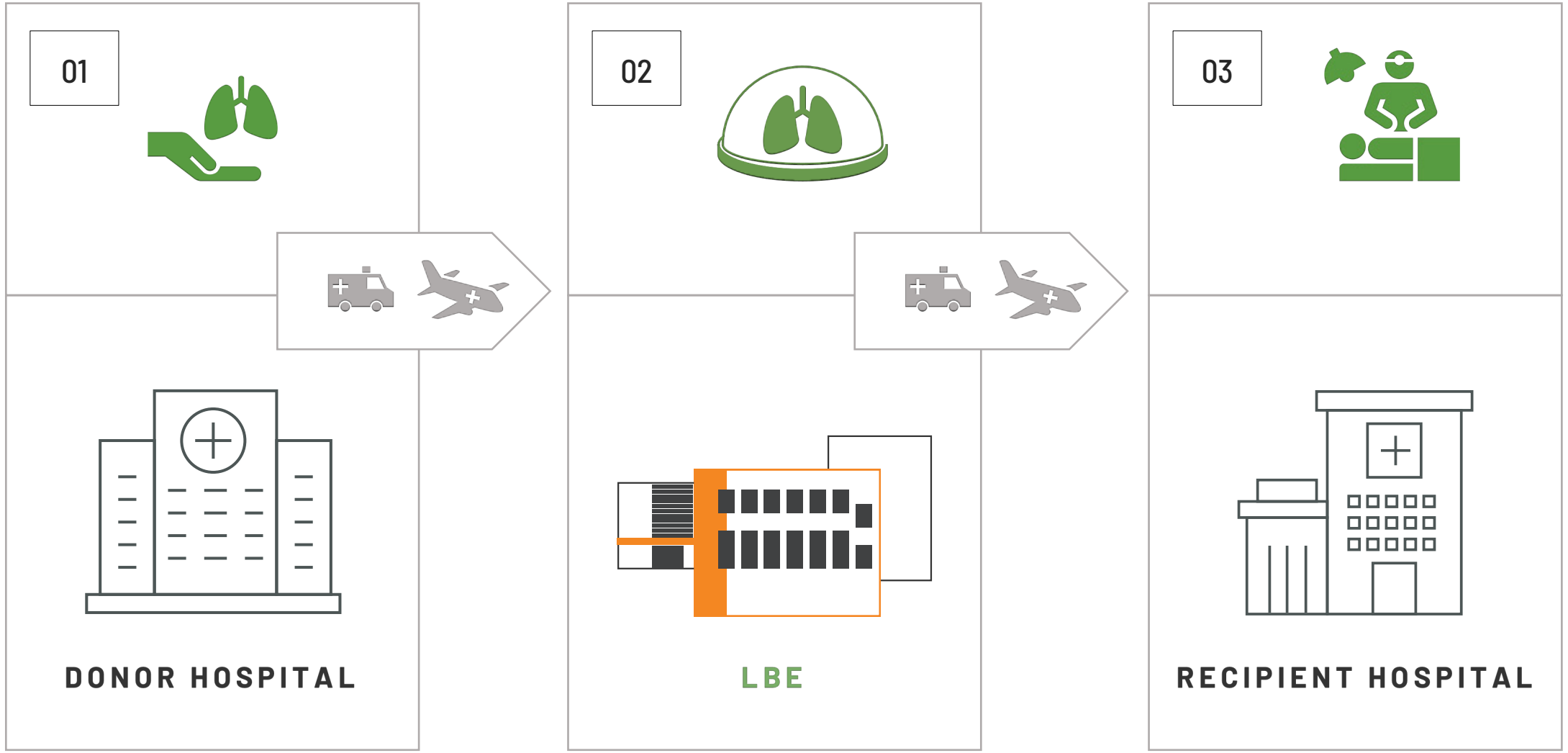


FDA APPROVED MEDICAL DEVICE

CASE MANAGEMENT & DATA SHARING/ REPOSITORY

LBE's Centralized EVLP Process

WHAT WE DO



Benefits of LBE Centralized EVLP service

REASONS TO BELIEVE

01 ROBUST EXPERTISE

02 FLEXIBILITY

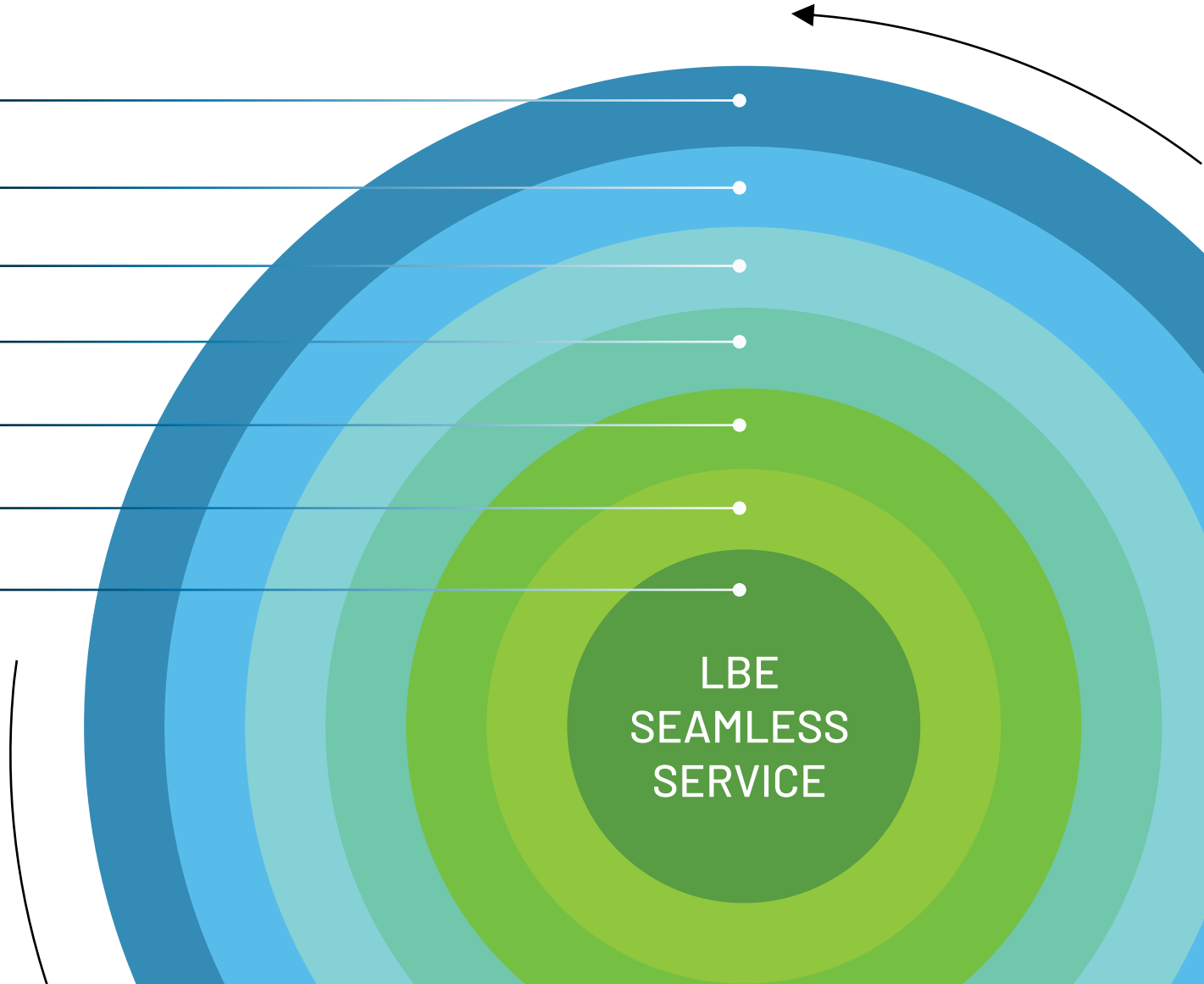
03 TRUSTWORTHY DATA

04 EXPANDED DONOR POOL

05 RESOURCE SAVINGS

06 RISK MANAGEMENT

07 CONTINUOUS LOGISTICAL ASSISTANCE



REASONS TO BELIEVE

LBE
SEAMLESS
SERVICE
BENEFITS

01

ROBUST EXPERIENCE

Our EVLP procedure figures as of September 16th, 2021*

291 **DONOR LUNGS**
AT **LB1** IN SILVER SPRING, MD &
LB2 IN JACKSONVILLE, FL

188 **EVLP LUNGS**
ACCEPTED TO TRANSPLANT

191 **PATIENTS**
TRANSPLANTED WITH EVLP LUNGS

Collective experience of our team

100+ **YEARS OF LBE CLINICAL TEAM EXPERIENCE**
IN DONATION, TRANSPLANTATION AND EVLP

Qualifications

Our EVLP Specialists undergo extensive training in collaboration with Toronto General Hospital where the technology was pioneered.

***The majority of procedures were done as part of a clinical trial using an investigational EVLP device.**

REASONS TO BELIEVE

LBE
SEAMLESS
SERVICE
BENEFITS

OUR EVLP TEAM

UNRIVALLED EXPERIENCE

24/7/365 AVAILABILITY

QUALITY ASSURANCE

REASONS TO BELIEVE

LBE
SEAMLESS
SERVICE
BENEFITS

02

FLEXIBILITY

OPTIMIZED DECISION MAKING

Extended preservation time provides transplant clinicians with additional opportunities to:

- evaluate lung viability
- ensure donor compatibility

while removing some of the resource burden on transplant center staff when lungs become available.

SINGLE OR DOUBLE LUNG EVLP

Our technology provides the ability to carry out double or single lung procedures.

IMPROVED PLANNING

EVLP allows flexibility in scheduling of transplant procedures for physicians and patients.

REDUCED TRAVEL

Utilizing LBE centralized service allows for assessment of lungs procured by other teams, ultimately decreasing dry runs by transplant centers' explant teams.

REASONS TO BELIEVE

LBE
SEAMLESS
SERVICE
BENEFITS

03

TRUSTWORTHY DATA

REMOTE REAL-TIME DATA

The case management exchange (XMX) provides transplant physicians with real-time data that is viewable remotely from any location and on any mobile device (including cellphones and tablets).

ENHANCED INSIGHT & COMMUNICATION

Live video and continuous data sharing at your fingertips allows for real-time lung evaluation and assessment with EVLP Specialists.

CONSISTENT INFORMATION

Data, radiographs, and high definition video of the procedure including bronchoscopies are consistently captured and shared, an advantage which often isn't available during lung evaluation in the donor ICU.

HISTORICAL REPOSITORY

Easy access to data, images, and video from previous cases in order to support learned decision making.

MEDICAL CONSULTANCY

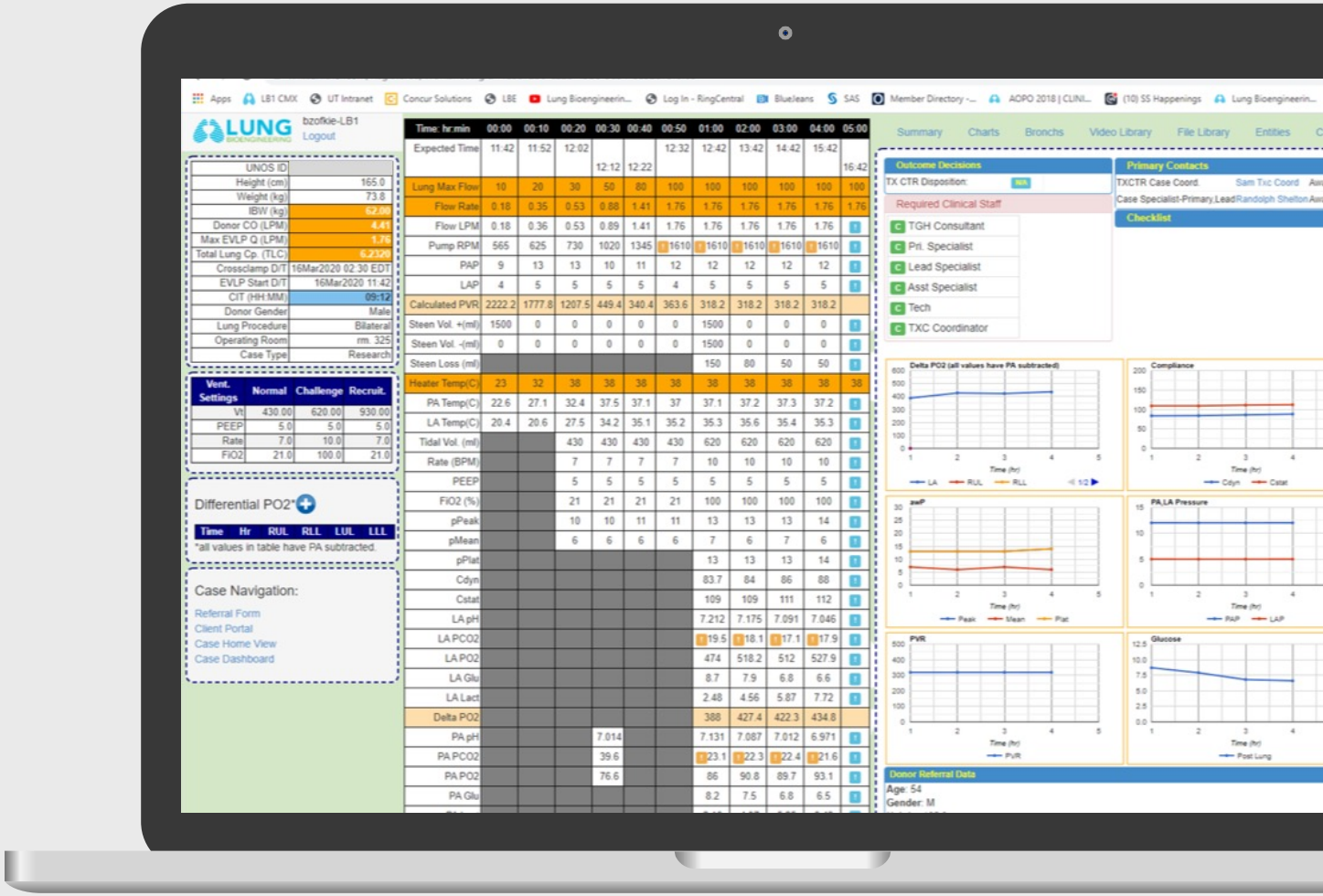
Medical consultations, from transplant physicians with experience using STEEN Solution™ based EVLP technology, are available during the procedure for peer-to-peer discussions.

REASONS TO BELIEVE

LBE
SEAMLESS
SERVICE
BENEFITS

ACCESS XMX ANYWHERE & ANYTIME

VIA INTERNET CONNECTION



REASONS TO BELIEVE

LBE SEAMLESS SERVICE BENEFITS

04

EXPANDED DONOR POOL

IMPROVES CHANCES FOR PATIENTS TO RECEIVE A LUNG THROUGH:

ACCESS TO ADDITIONAL DONOR LUNGS

EVLP allows for consideration of lungs that once would have gone unused, such as those with limited or suspect functional data, or from more distant donor hospitals.

MULTIPLE EVLP PROCEDURE ROOMS

LBE has two centers with four devices, ensuring access to EVLP services 24/7/365.

UTILIZATION OF LUNGS FROM NON-TRADITIONAL CASES

- Intraoperative referrals
- DCDs
- Double lung perfusion to single lung recipients
- Other transplant center procurement teams

REASONS TO BELIEVE

LBE
SEAMLESS
SERVICE
BENEFITS

OUR FACILITIES

- ✓ CONTROLLED ENVIRONMENT
- ✓ IN-HOUSE MATERIALS AND INVENTORY
- ✓ FACILITIES WITH AV INTEGRATION
- ✓ 24/7/365 AVAILABILITY

SILVER SPRING, MD

28,000 ft^2 facility | Six procedure rooms

JACKSONVILLE, FL

25,000 ft^2 facility | Three procedure rooms

REASONS TO BELIEVE

LBE
SEAMLESS
SERVICE
BENEFITS

05

REDUCED RESOURCE BURDEN

REDUCTION OF RESOURCE BURDEN

Lung Bioengineering's centralized EVLP model reduces the resource burdens experienced with in-house EVLP which include:

- Costs of personnel, training, and equipment
- Technical issues that can occur during learning curve of training or in circumstances where EVLP technology is not regularly used
- OR time
- Expiring consumables inventory

Additionally, EVLP may increase the number of lungs available for transplant, thereby reducing the number of days patients wait for organs. In turn, this could lower pre-transplant costs of care by shortening the time some transplant recipients spend in the hospital and intensive care unit (ICU) waiting for a donor.

REASONS TO BELIEVE

LBE
SEAMLESS
SERVICE
BENEFITS

06

RISK MANAGEMENT

FACILITATION OF FURTHER EVALUATION

Lungs are assessed in an ex vivo environment which allows for the gathering of information that may not be available in the ICU. This means that lungs can be sent for further evaluation, even on short notice, and provides transplant physicians with greater confidence in their decision making.

POSSIBILITY OF REALLOCATION

Our model allows for the reallocation of lungs while on EVLP, maximizing the potential for lungs to go to transplant.

REASONS TO BELIEVE

LBE
SEAMLESS
SERVICE
BENEFITS

07

CONTINUOUS LOGISTICAL ASSISTANCE

CONTINUOUS EXPERT SUPPORT

LBE's experienced EVLP Specialists understand the medical management of donor lungs, the allocation system, and transportation logistics and are on hand to offer support throughout the EVLP process.

BENEFICIAL FEEDBACK PROCESS

LBE's feedback process can help to align center lung explant protocols, creating further consistency within the industry.

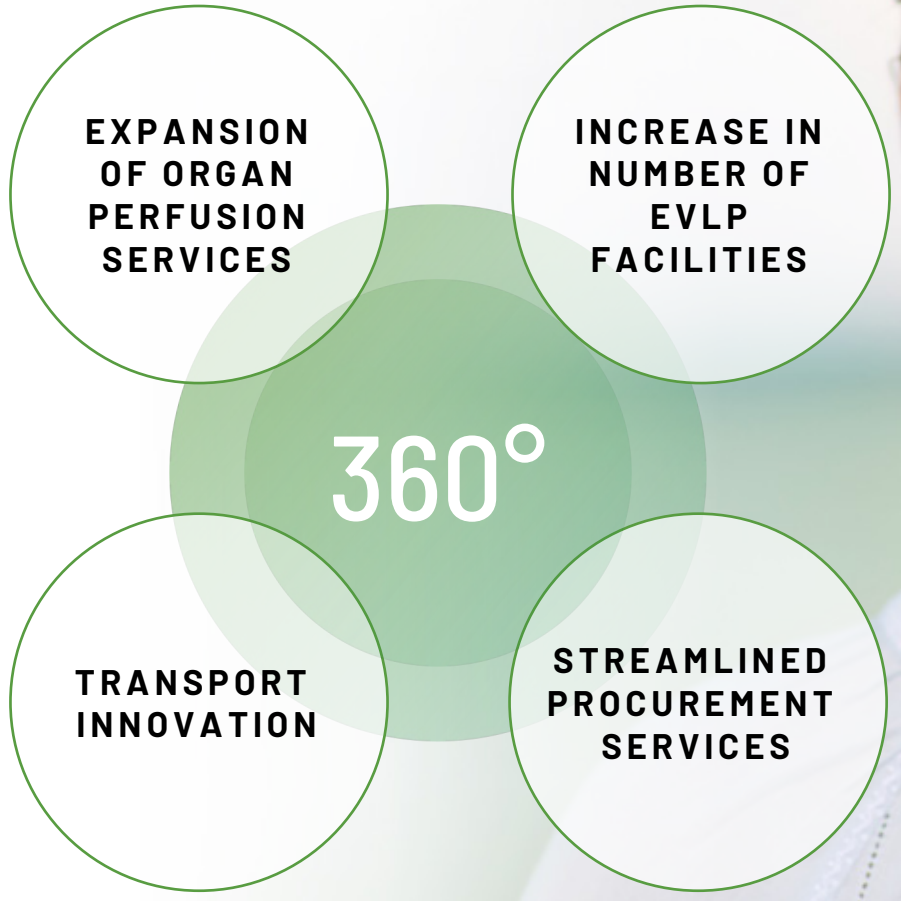
Lung Bioengineering 360°

THE FUTURE OF OUR CENTRALIZED EVLP MODEL

WHAT WE DO

As we work towards the future, we are expanding our capabilities to deliver a true 360-degree service model for organ transplantation. This model will encompass hearts, kidneys, livers, and lungs in addition to broadening the transplantation services and technologies we offer.

Our services will evolve over time, from assisting in logistics and providing real-time access to data today, to facilitating procurement, and supporting therapeutic advancements in the future.



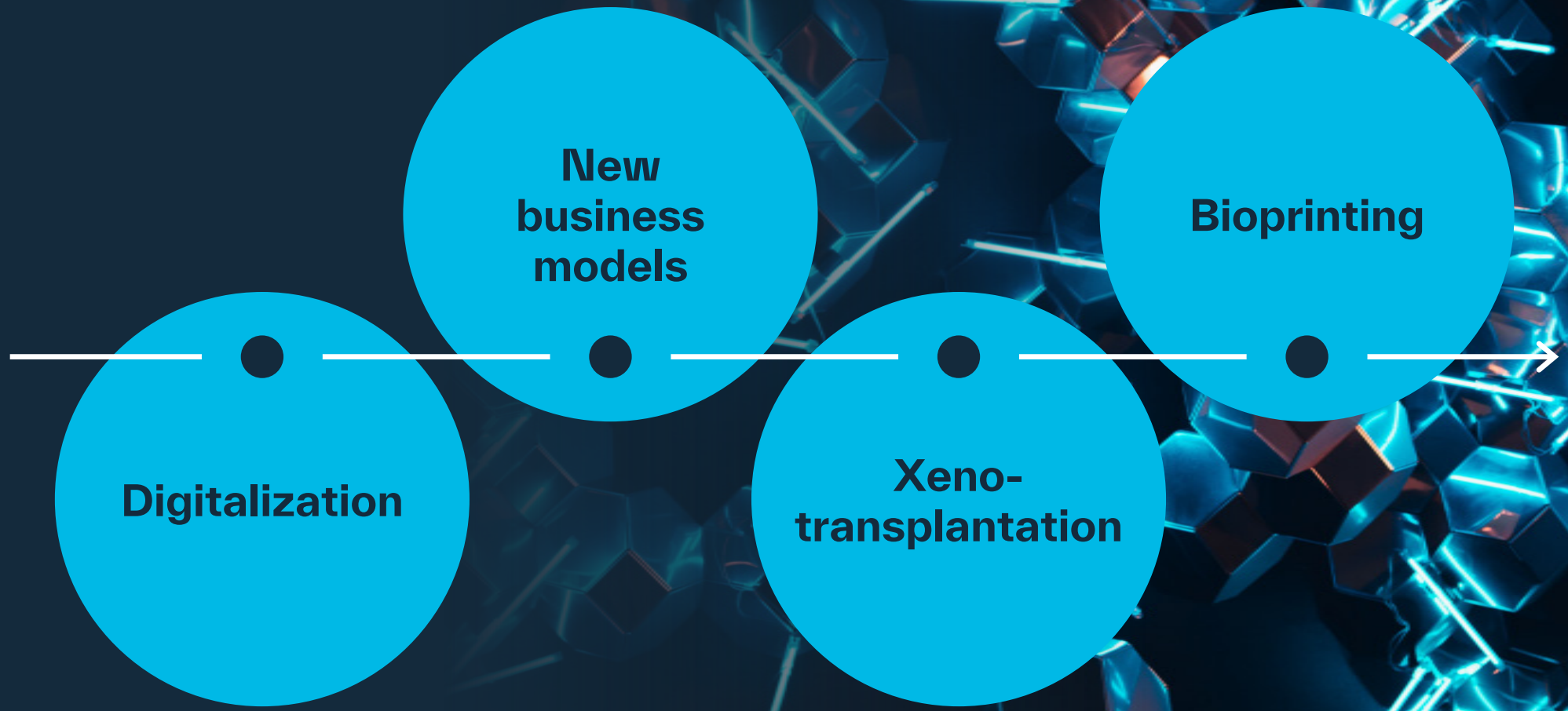
THANK YOU

Future of transplantation

Christoffer Rosenblad, COO

XVIVO

Megatrends in transplantation



Xenotranplantation

Prof. Muhammad M. Mohiuddin
University of Maryland School of Medicine

XVIVO

UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE

Cardiac Xenotransplantation

Muhammad Mansoor Mohiuddin, MBBS

Professor of Surgery

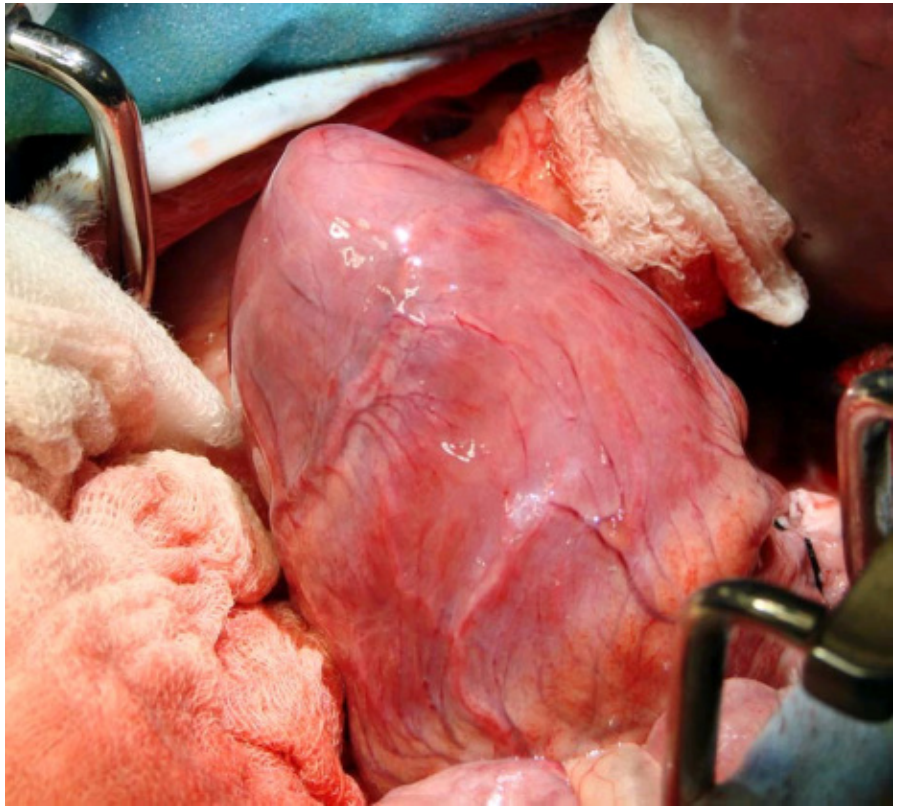
Director, Program in Cardiac Xenotransplantation

Department of Surgery, Division of Cardiac Surgery

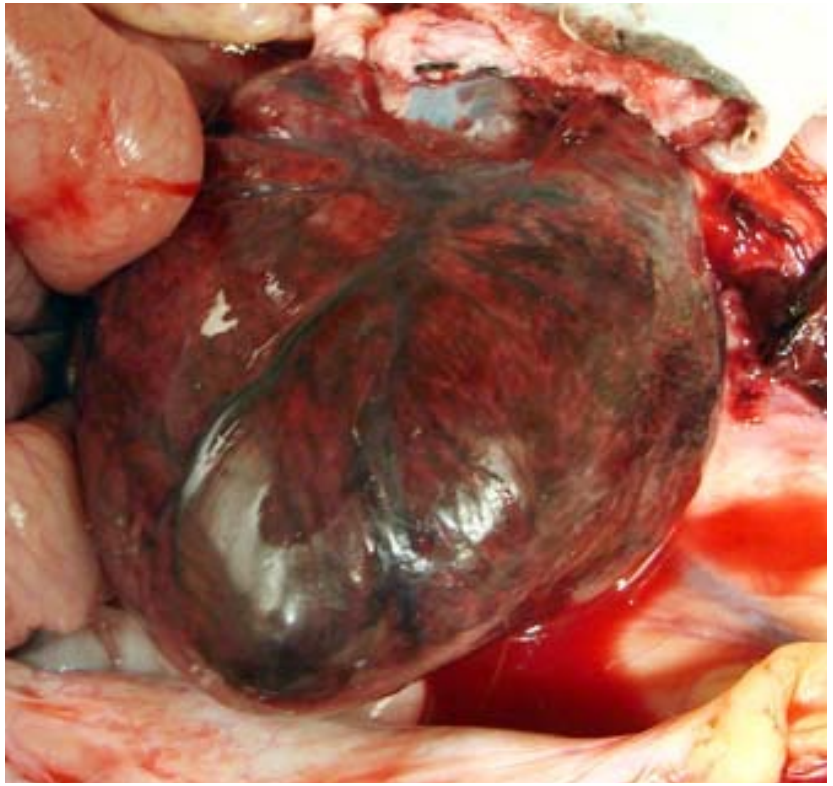
University of Maryland School of Medicine

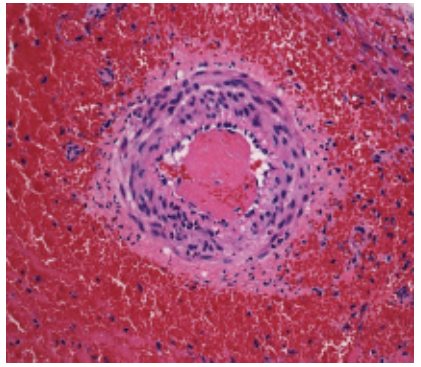
Baltimore, Maryland, USA

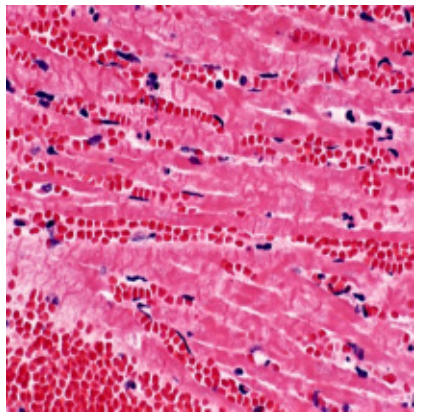
Normal Xenograft



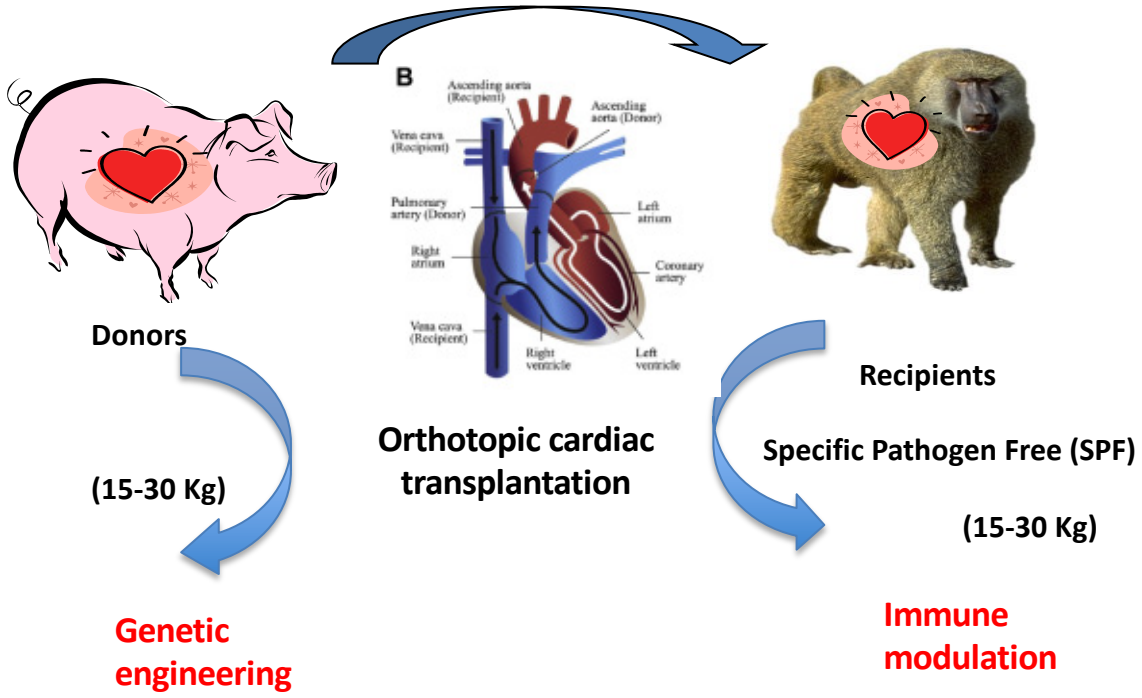
Hyper Acute Xenograft Rejection (HAR) Within Minutes



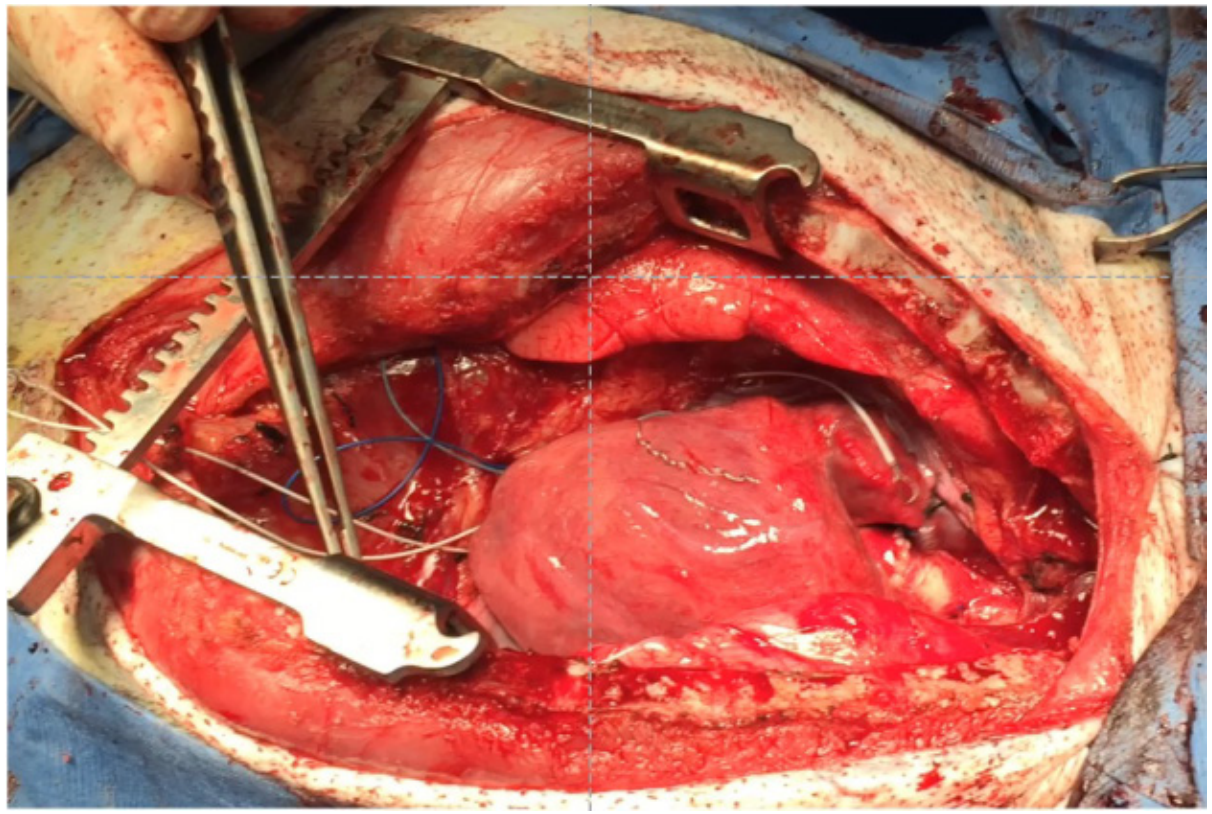




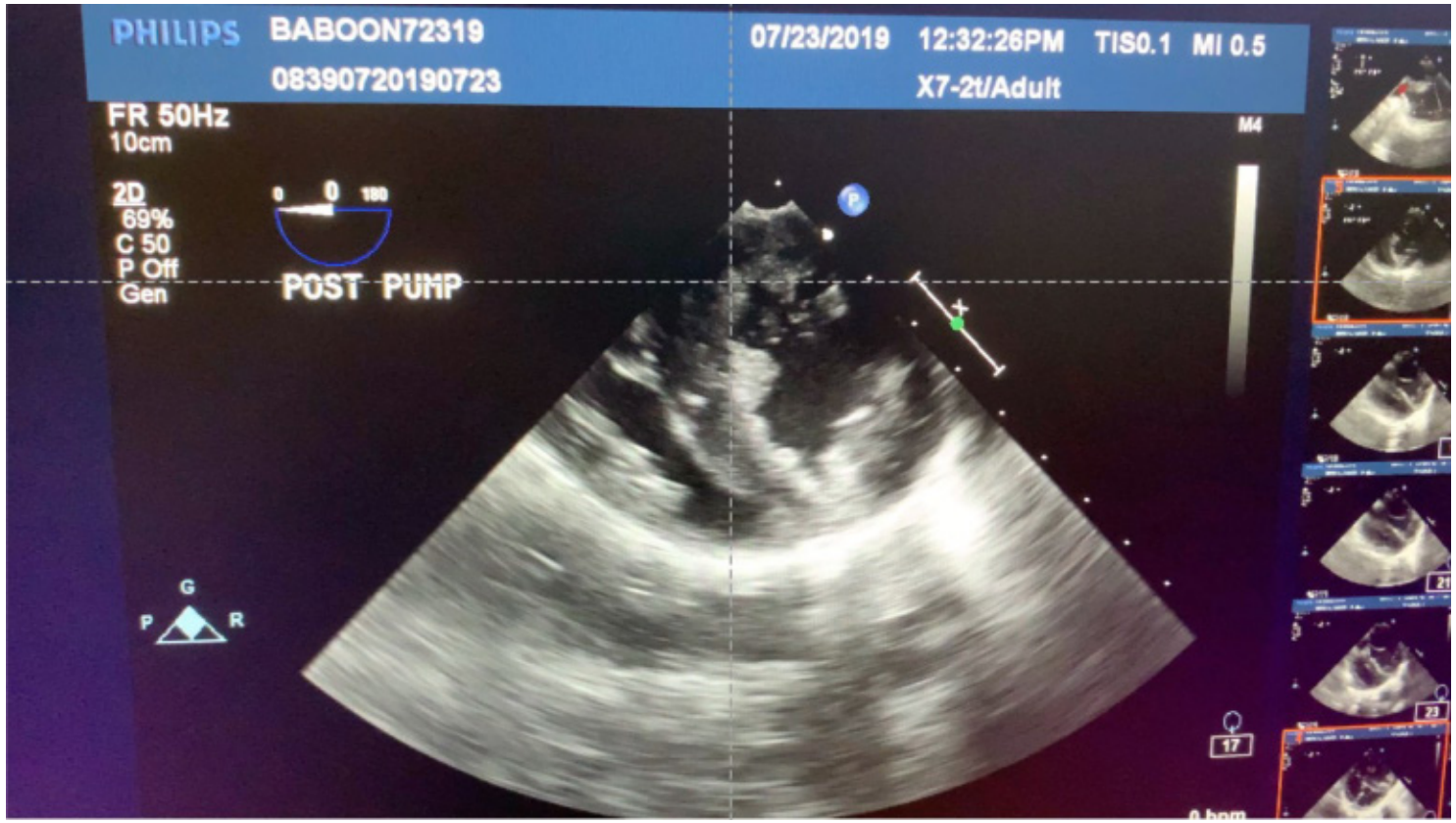
Orthotopic Tx



Orthotopic Transplant

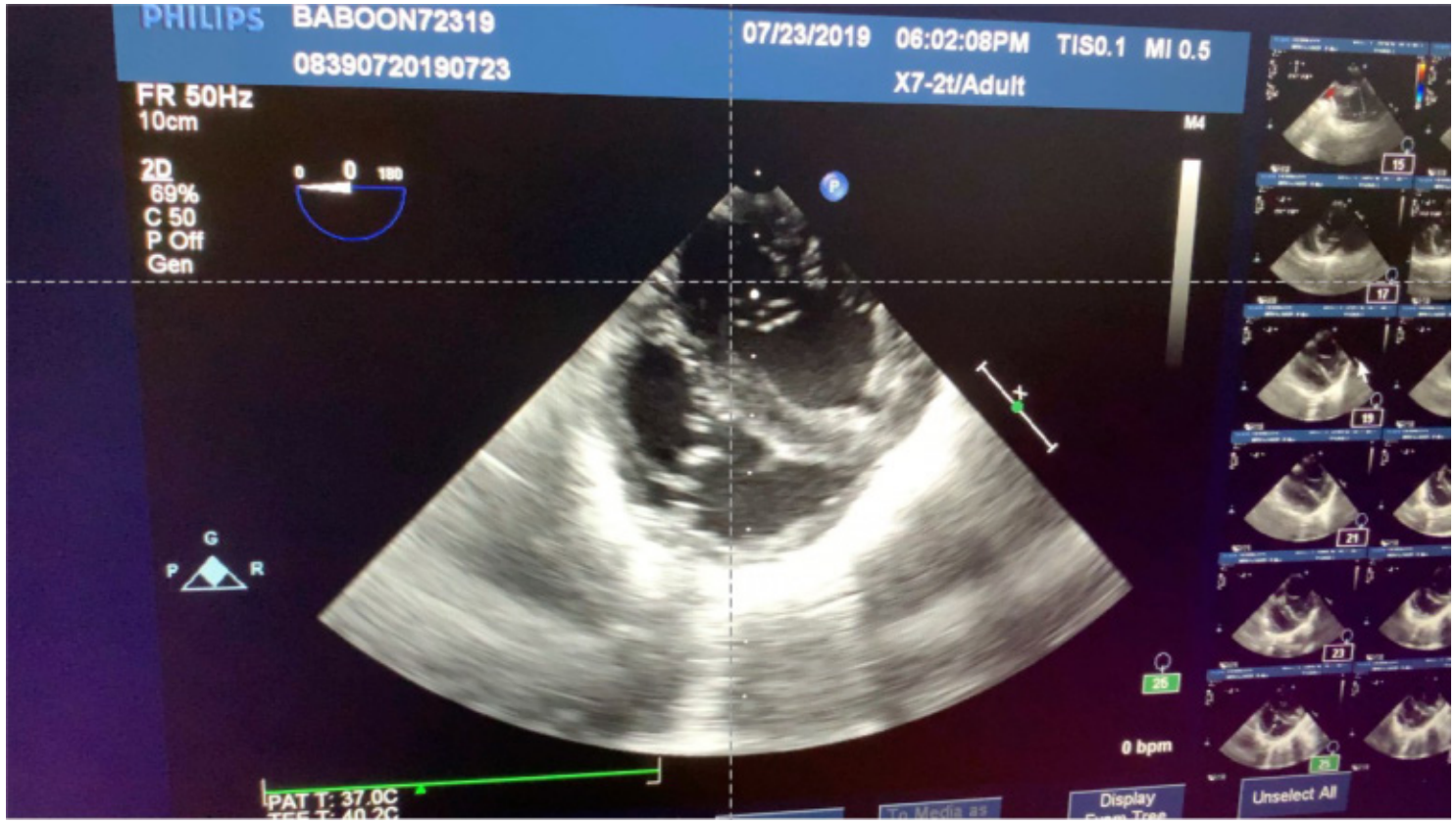


Postoperative Cardiac Xenotransplant Function



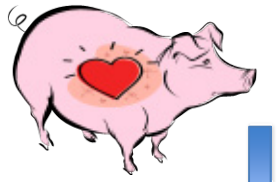
Coming off of bypass

Postoperative Cardiac Xenotransplant Function



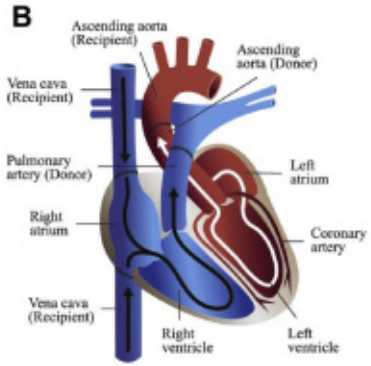
5 hours post-bypass

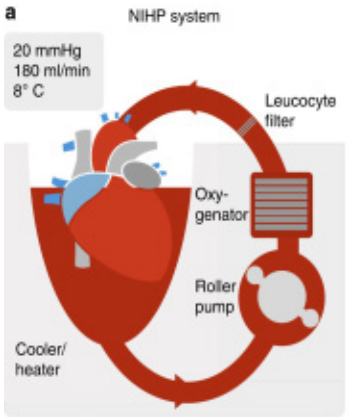
Model



XVIVO Heart Box

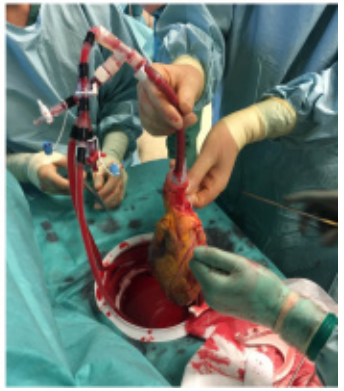
Orthotopic transplant





b Heart preservation solution

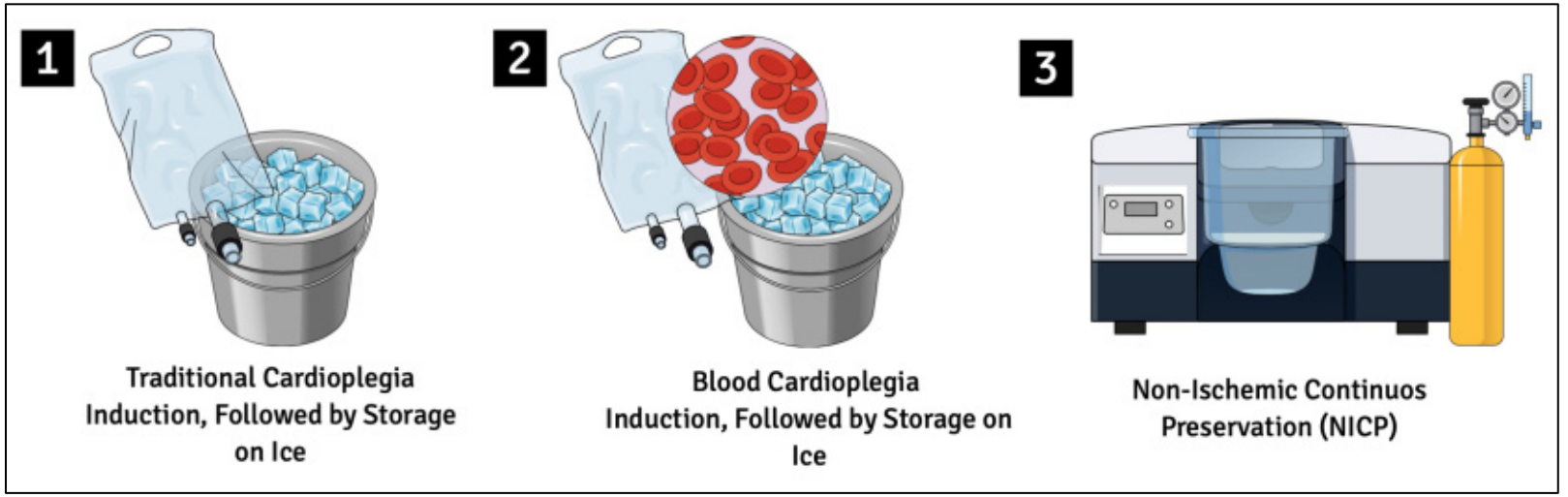
Sodium (Na^+)	136 mmol/L
Potassium (K^+)	23 mmol/L
Calcium (Ca^{2+})	1.3 mmol/L
Magnesium (Mg^{2+})	8.0 mmol/L
Chloride (Cl^-)	142 mmol/L
Bicarbonate (HCO_3^-)	25 mmol/L
Phosphate (PO_4^{2-})	1.3 mmol/L
D-Glucose	6.3 mmol/L
Albumin	75 g/L
Dextran-40	1 g/L
Cocaine	6 nmol/L
Noradrenaline	6 nmol/L
Adrenaline	6 nmol/L
Triiodothyronine (T3)	3 nmol/L
Cortisol	420 nmol/L
Insulin	8 U/L
Imipenem	20 mg/L
Erythrocytes (Hct)	15%
95% O_2 + 5% CO_2	0.2 L/min



Thanks to Prof. Bruno Reichart' s Group

Methods

- Donor genetically modified cardiac xenografts from landrace pigs were transplanted into *Papio albus* recipients.
- After procurement and prior to transplantation, one of the following induction/preservation techniques were employed:



Methods

Support Scale	1	2	3	4	5
Inotropes:					
Epinephrine (mcg/kg/min)	0.01-0.05	0.06-0.01	0.11-0.15	0.16-0.20	> 0.20
Dobutamine (mcg/kg/min)	2.5-6.9	7.0-11.4	11.5-16.9	16.0-20.4	> 20.4
Milrinone (mcg/kg/min)	0.125-0.24	0.250-0.374	0.375-0.49	0.5-0.624	> 0.624
Vasopressors:					
Norepinephrine (mcg/kg/min)	0.01-0.1	0.11-0.2	0.21-0.3	0.31-0.4	> 0.4
Phenylephrine (mcg/kg/min)	0.1-0.9	1.0-1.9	2.0-2.9	3.0-4.0	> 4.0
Vasopressin (units/min)	0.01	0.02	0.03	0.04	> 0.04

Results

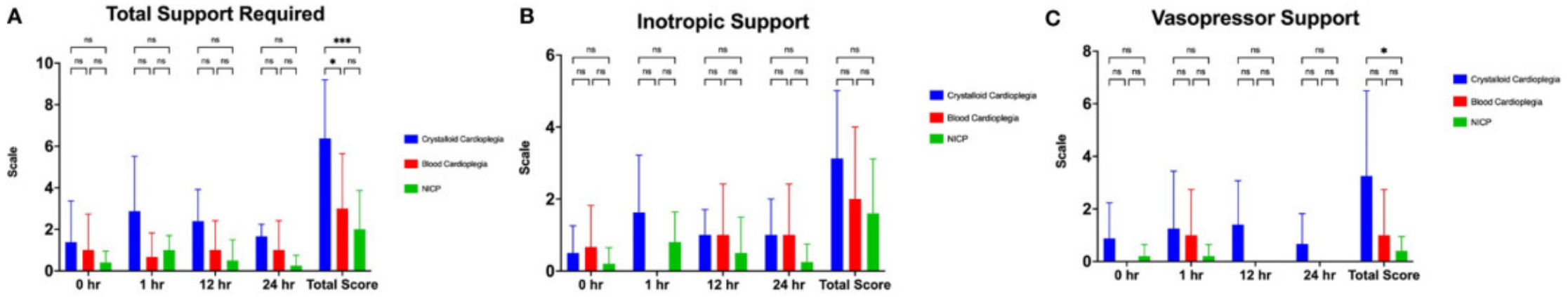
Genetics	Preservation Type	Donor weight (kg)	Recipient weight (kg)
GTKO.B4KO.hCD46.hTBM.hEPCR.hCD47.hHO1.hVWF	Crystalloid Induction with Slush Storage	21	25
GTKO.hCD46.hTBM.hCD47.hEPCR.hHO1		10	10
GTKO.hCD46.hTBM.hCD47.hEPCR.hHO1		23	21
GTKO.hCD46		13	13
GTKO.B4KO.hCD46.hHLAE		9	10
GTKO.CMAHKO.hCD46.hCD47.hTFPI		20	18
GTKO.CMAHKO.hCD46.hEPCR.hDAF.hTBM.hHO1		20	20
GTKO.hCD46.hTBM		29	30
GTKO.hCD46.hTBM	Blood Cardioplegia Induction with Slush Storage	12	13
GTKO.hCD46.hTBM		20	17
GTKO.hCD46.hTBM		21	21
TKO.hCD46.hDAF	Non-Ischemic Continuous Preservation	18	22
TKO only		24	23
GTKO.hCD46.hTBM		21	22
GTKO.hCD46.hTBM		16	16
GTKO.hCD46.hTBM		21	30

Results

Preservation Type	% Extubated	% Surpassed PCXD	Total Support	Peak Lactate	Peak Base Deficit	Peak pH
Traditional (n=8)	0.0%	0.0%	6.4 ± 2.8	14.3 ± 1.7	12.5 ± 4.9	7.19 ± 0.1
Blood Cardioplegia (n=3)	66.7%	66.7%	3.0 ± 2.6	3.6 ± 0.0	4.3 ± 3.0	7.29 ± 0.2
NICP (n=5)	100.0%	80.0%	2.0 ± 1.9	3.5 ± 1.5	3.9 ± 1.8	7.33 ± 0.06

Blood cardioplegia and XHS (NICP) overcome PCXD Compared to Crystalloid Cardioplegia

- Blood Cardioplegia/NICP (Steen) better than crystalloid cardioplegia
- **Primary end point:** surpassed PCXD (dotted line)
- **Secondary end point:** amount of support required, metabolic derangements



Goerlich, C. E. et al. Blood Cardioplegia Induction, Perfusion Storage and Graft Dysfunction in Cardiac Xenotransplantation. Front. Immunol. 12:667093, (2021).

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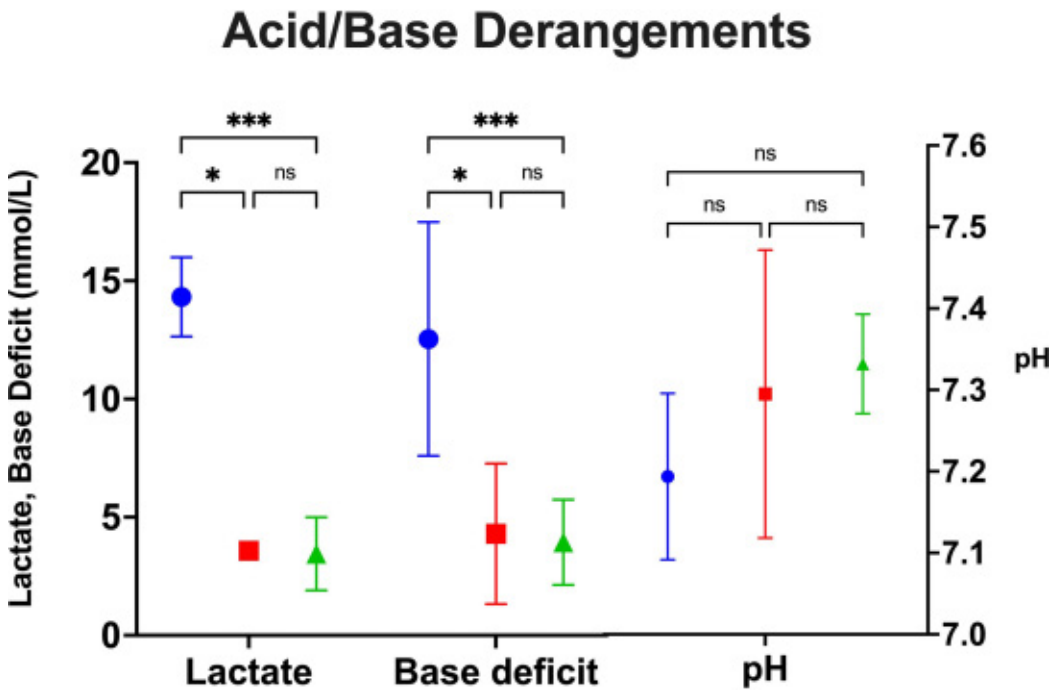

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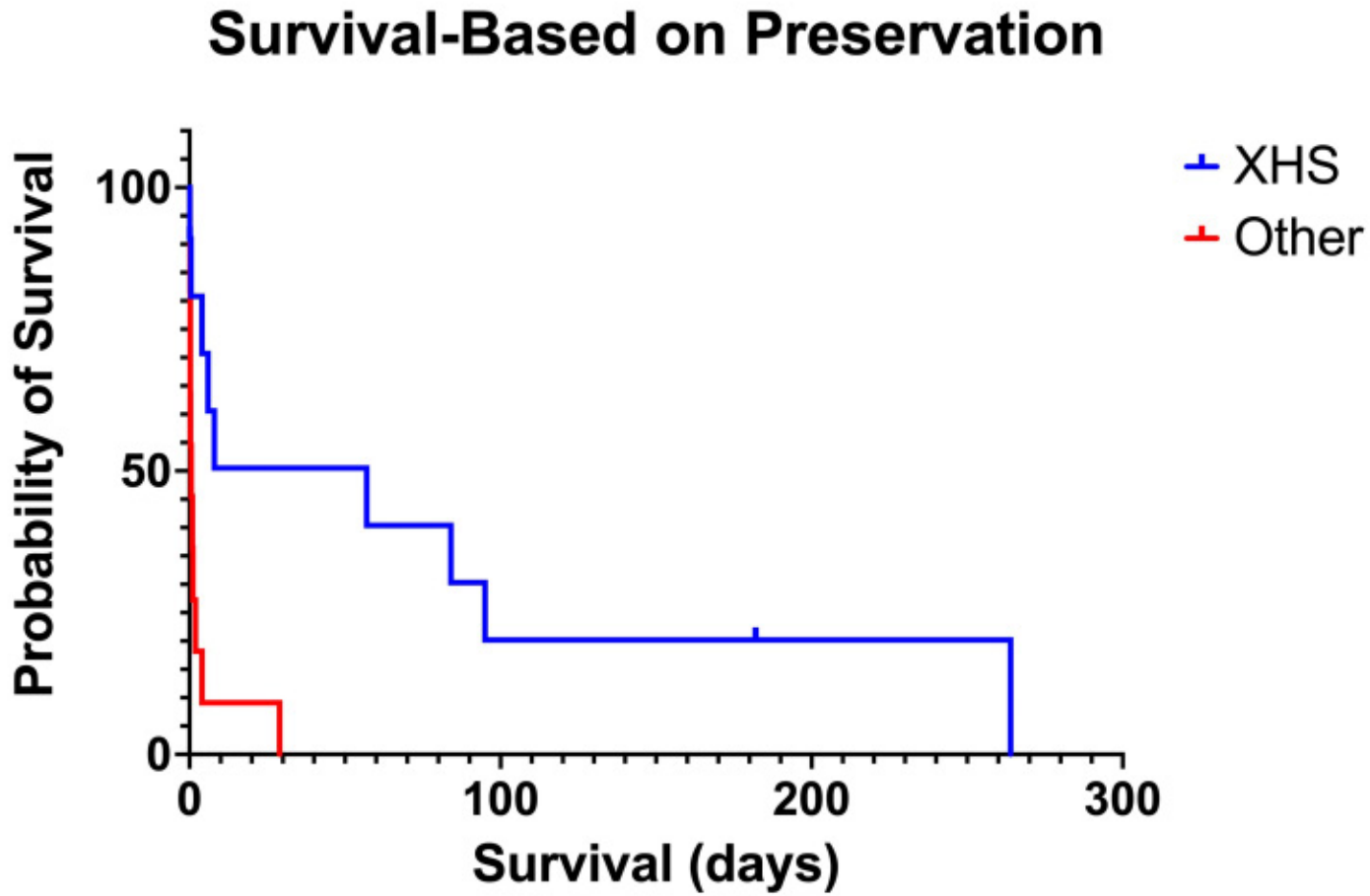
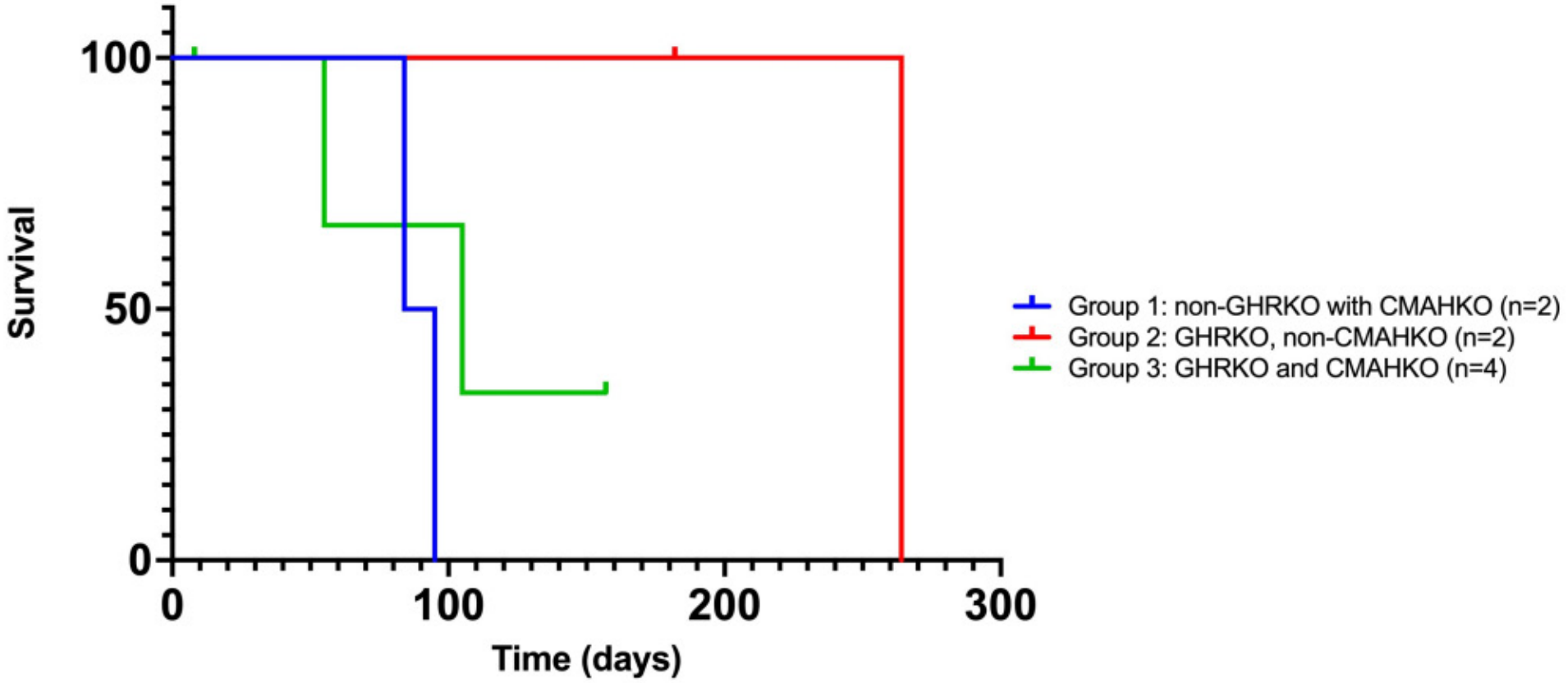

Survival-Based on Preservation
Probability of Survival
100
50
0
0
100
200
300
Survival (days)
XHS
Other

Results: Graft Survival



Conclusions

- **Graft survival is minimal with conventional methods of cardioplegia and preservation**
- **PCXD limits graft survival beyond 48 hours**
- **All transplants performed with XVIVO XHS and heart box overcame PCXD**
- **Heart Xeno and Allografts after NICP did not require any inotropic support and had almost no complications after extubation.**
- **All our long-term graft survivals utilized XVIVO heart box .**
- **Looking forward to use it in our human transplants . Both Allo and Xeno.**

UNIVERSITY of MARYLAND
SCHOOL OF MEDICINE

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David Kaczorowski

Immunologist
Avneesh Singh

Residents
Corbin Goerlich

Anesthesiologist
Eric Strauss
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Perfusionists
Brian McCormick
Brian Donahue
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Lauren Szostek
Sarah Mudd

Cardiologists
Anuj Gupta

Intensivist
Adnan Bhutta
Ali Tabatabai

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Ivan Tatarov

Surgeon
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Research Fellows
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Revivicor Inc
David Ayares

Sponsors:
United Therapeutics, Inc / Lung Biotechnology, Inc./ Revivicor Inc., USA
National Institute of Allergy and Infectious Diseases / National Institutes of Health, USA

Thanks

Key take-aways: Future of transplantation

- Today 10% of the total need for organ transplant is met
- Machine perfusion is proven to increase the number of transplantable organs
- New business models and Innovation e.g. Xeno transplantation will play a vital role to one day accomplish our vision that “Nobody should die waiting for a new organ”

Q&A


Thank you
Dag Andersson, CEO

In summary

- A global organ shortage
- Focus on organ utilization is increasing
- Machine perfusion recognized as the enabler to drive utilization
- XVIVO has a unique range of products for all major organs
- Execution of our five strategic focus areas will make us the global leading ‘all organ’ company

XVIVO

Nobody should die waiting for a new organ

Thank you!

Glossary

Clinical study / trial
A study in healthy or sick people to study the effect of a drug or treatment method.

DBD
Donation after brain death.

DCD
Donation after circulatory death.

DHOPE
Dual hypothermic oxygenated machine perfusion.

Durable goods
Revenues from the sale or rental of machinery for mechanical perfusion and preservation of organs.

Evaluation
Evaluation of the function of an organ.

EVLP or (Ex Vivo Lung Perfusion)
Perfusion of a lung outside the body. The procedure is normally done to evaluate a lung before transplantation.

Ex vivo (Latin for "outside a living organism")
Biological processes in living cells and tissues when they are in an artificial environment outside the body. "Opposite" of in vivo.

FDA or US Food and Drug Administration
The FDA is the US's food and drug authority with responsibility for food, dietary supplements, drugs, cosmetics, medical equipment, radiology equipment, and blood products. FDA approval is required to market a medical device on the US market.

HMPO2
Oxygenated hypothermic machine perfusion.

Hypothermic nonischemic perfusion of heart
Circulation of the cooled, dormant donated heart with supply of oxygen and necessary nutrients during transport to the recipient.

Hypothermic perfusion
Perfusion at temperatures < normal body temperature.

KOL
Key Opinion Leader.

Machine perfusion
New technology that improves preservation and evaluation of organs, which means more organs can be used for transplants. In the Thoracic business area this includes STEEN Solution™, XPS™, LS™ and Lung Assist. In the Abdominal business area this includes Kidney Assist Transport, Kidney Assist and Liver Assist as well as other products and services related to the use of those machines.

Glossary

NEJM
New England Journal of Medicine.

NHSBT
The NHS (National Health Service) Blood and Transplant in UK.

NICE
The National Institute of Health and Care Excellence in the UK.

NIHP
Nonischemic heart preservation.

Non-durable goods
Revenues from the sale of disposables and solutions for machine perfusion and static preservation.

Normothermic perfusion
Perfusion at temperatures at normal body temperature.

OPO or Organ Procurement Organization
In the United States, an organ procurement organization (OPO) is a non-profit organization responsible for the evaluation and procurement of deceased donor organs for organ transplantation. There are approximately 58 such organizations in the United States.

Perfusion
Passage of a fluid through an organ's blood vessels.

PMA or Premarket Approval
Premarket approval (PMA) is the FDA - process of scientific and regulatory review to evaluate the safety and efficacy of a medical device.

Preclinical study
Research performed before a drug or method of treatment is sufficiently documented to be studied in humans.

Preservation
Storage and maintenance of an organ outside the body before transplantation.

Reimbursement
Reimbursement is used in the health insurance system in order for healthcare providers to be reimbursed faster and more easily for accrued expenses from a private or public insurance company (in the United States, e.g. Medicare).

Static preservation
Static preservation refers to preservation methods where the organ is cooled during transport and before transplantation. In the Thoracic business area, this includes PERFADEX® Plus as well as other products and services related to the use of that product.

Xenotransplantation
Transplantation of living cells, tissues or organs from one species to another.