CONFIDENTIAL

DIALYBRID

Revolutionizing the World of Grafts

Pitch Deck

January 2023

Table of Contents

DIALYBRID

Snapshot on Dialybrid

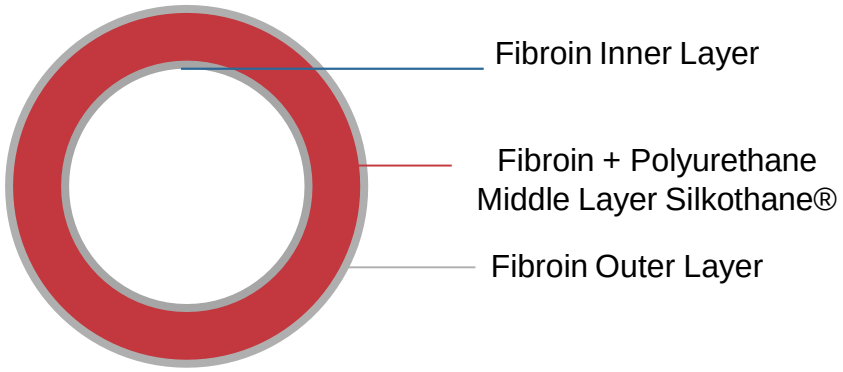
Project Overview

- Dialybrid® is an innovative research project related to the development of a new biomaterial for cardiovascular grafts
- The proprietary material, called Silkothane®, is composed of a natural degradable material (silk fibroin) and a non-degradable synthetic material (polyurethane)
- The key characteristics of Dialybrid®'s solution are: (i) biocompatibility, (ii) elasticity and stability, (iii) off-the-shelf availability, (iv) tuneability of mechanical properties and (v) resistance to infections
- The identified first application is to use the Silkothane® to develop an arteriovenous graft, which is used in dialysis to connect an artery to a vein

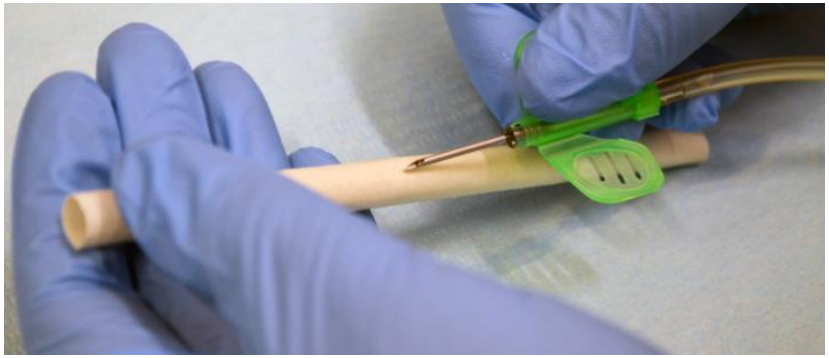
Silkothane® Key Characteristics

Characteristics	Description
Biocompatible	Feature derived from the silk fibroin material
Elastic and Stable	Feature derived from the polyurethane
Ready to use	Available off the shelf
Tunable	Possibility of matching the mechanical properties to final application
Resistant to infections	Unlike traditional grafts

Dialybrid® Graft Composition



Dialybrid® Graft Sample

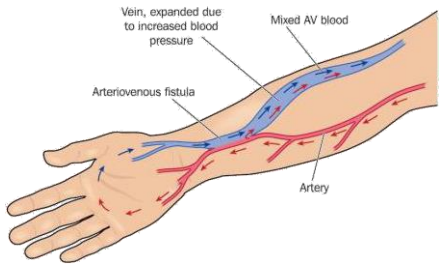


Source: Company information

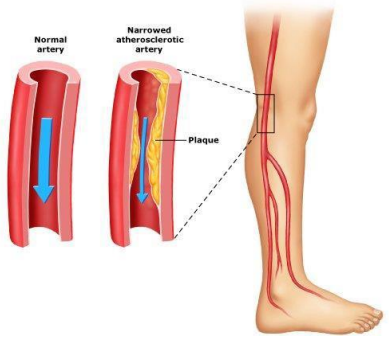
Dialybrid Graft Key Applications

DIALYBRID

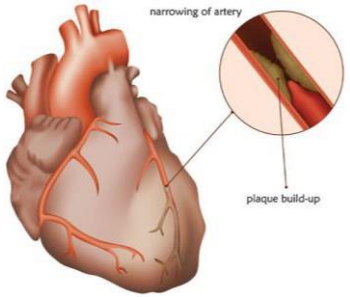
Dialysis Vascular Access



Peripheral Artery Disease (PAD)



Coronary Artery Disease (CAD)



Peripheral vascular system | **Central vascular system**

Limits of currently available solutions

Issue	Description
Material	Synthetic grafts generally feature poor biocompatibility, with consequent thromboses or chronic inflammation
Performances	Synthetic grafts fail in vessels with diameter < 6mm (e.g. **coronary arteries**), where native vessels (e.g. saphenous vein or mammary artery) need to be used In **peripheral applications** (e.g. PAD and hemodialysis), synthetic grafts fail due to poor patency and high infection rates, with burdensome maintenance costs
Availability	Native grafts (e.g. saphenous vein) are not always available and their withdrawal causes donor site morbidity
Compliance mismatch	Synthetic grafts are too rigid to fit the mechanical properties of native tissues and the compliance mismatch causes graft failure (e.g. patency loss)

Source: Company information

Patent portfolio

PCT/EP2017/001263

- priority 28.10.2016
- expiration 27.10.2037

EU patents

EU 17797522.4 ✓

- granted 14.10.2020
- expiring 27.10.2037
- Nationalized in 18 Countries (IT, AU, HR, DK, FI, FR, DE, GR, IE, NO, NL, PL, PT, GB, SI, ES, SE, CH)
- covering Silkothane® products (different geometries) and manufacturing process

EU 20201412.2 

- divisional application
- covering Silkothane® material itself (liquid and solid form)
- registered also in Hong Kong on 20.09.2021
- positive preliminary exam

US patents

USA 11213612B2 ✓

- granted 04.01.2022
- expiring 03.02.2038
- Continuation In Part
- covering Silkothane® products (different geometries) and manufacturing process with limitations (electrospinning only)

USA 17/397365 

- divisional application
- covering Silkothane® material itself (liquid and solid form)
- waiting for examination

Source: Company information

Table of Contents

Dialybrid Target Market includes peripheral and coronary diseases

DIALYBRID

	Dialysis Vascular Access	PAD	CAD
Application	Dialysis	Peripheral revascularization	Coronary (or cardiac) revascularization
Current treatment	▪ Synthetic arteriovenous grafts ▪ Fistulae ▪ CVC	▪ Synthetic grafts (GoreTex, Dacron) ▪ Angioplasty and stenting	▪ CABG (Coronary Artery Bypass Grafting) with native vessels ▪ Percutaneous coronary intervention (PCI) ▪ Angioplasty and stenting
Dialybrid offer	Arteriovenous graft ("AV graft")	Hybrid peripheral (stent) graft	Coronary (stent) graft
Global Market Value (2025E)	**$1.2bn**	**$3.1bn**	**$7.9bn**

Dialybrid plans to initially target the +$600m EU and US dialysis vascular access market, which accounts for c.50% of the global market

Source: Company Information

Dialybrid First Target Market: Dialysis Vascular Accesses

DIALYBRID

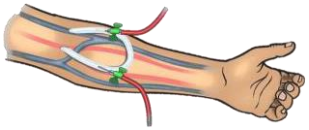
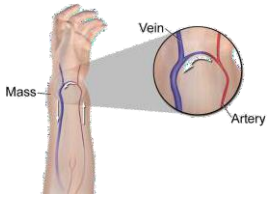
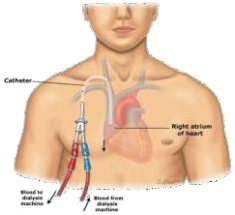
Why Dialysis first?

1	**Clear market Need**	▪ Currently available alternatives of dialysis vascular **accesses fail in approximately 40-50% of the cases within 1 year**, due to the formation of aneurisms, thrombi, or infective complications ▪ These failures have a tremendous impact on the quality of life of dialytic patients and are **extremely burdensome in terms of costs associated to vascular access maintenance** (estimated to be $2.8bn in US in 2013)(1)
2	**Lower risk compared to alternative markets**	▪ Dialysis is a lower-risk market compared to others (e.g., coronary stents) since dialytic patients are **regularly monitored** by physicians 3 times per week, and possible unforeseen events (e.g., thromboses) pose **lower-impact complications** (i.e., ischemia of the hand, rather than cerebral or cardiac ischemias)
3	**Lower investments needed**	▪ As a consequence of the lower risk, **clinical studies in the dialysis field are less expensive than in other fields**
4	**Viable as test bed for further applications**	▪ **Dialysis requires the graft to be punctured**. As a consequence, the graft needs to be able to **support significant stress** ▪ For this reason, a graft used to perform dialysis is most likely to be **viable for other less-stressful applications** as well

Dialybrid's first application – Dialybrid's AV graft – will be a test-bed for future applications

Source: Company information; Note (1): Thamer, Mae et al. (2018). Medicare Costs Associated With Arteriovenous Fistulas Among US Hemodialysis Patients. American Journal of Kidney Diseases

Dialysis Vascular Accesses Current Solutions & Market Value

Product	# of EU-US yearly units(2)	EU-US Market Value(2)	Description	Dialybrid Advantage
 **Synthetic Arteriovenous grafts**	**72,000**	**$181m**	Synthetic or tissue engineered protheses placed between a vein and an artery to create an "artificial" connection	▪ Lower incidence of occlusion and inflammatory issues ▪ Target price at Dialybrid in line with synthetic market standard (Acuseal)
 **Fistulae**	**184,000**	**$313m**	Direct surgical connections created between an artery and a vein, without any inorganic medical device	▪ Immediately accessible ▪ Same target complication rate since it adapts to body thanks to biocompatibility and remodelling
 **CVC**	**385,000**	**$116m**	CVC is adopted only in certain rare cases when urgent hemodialysis is needed. It is discouraged by guidelines	▪ Long term usability ▪ Lower target risk of infections
	Total:	**$610m**		

Current alternatives failure rate is equal to c.40% within the first year

Source: Company information; Note (1): Desai - Two-Year Outcomes of Early Cannulation Arteriovenous Grafts for End-Stage Renal Disease; Note (2): refers to 2025

Dialybrid is more effective along all considered variables

DIALYBRID

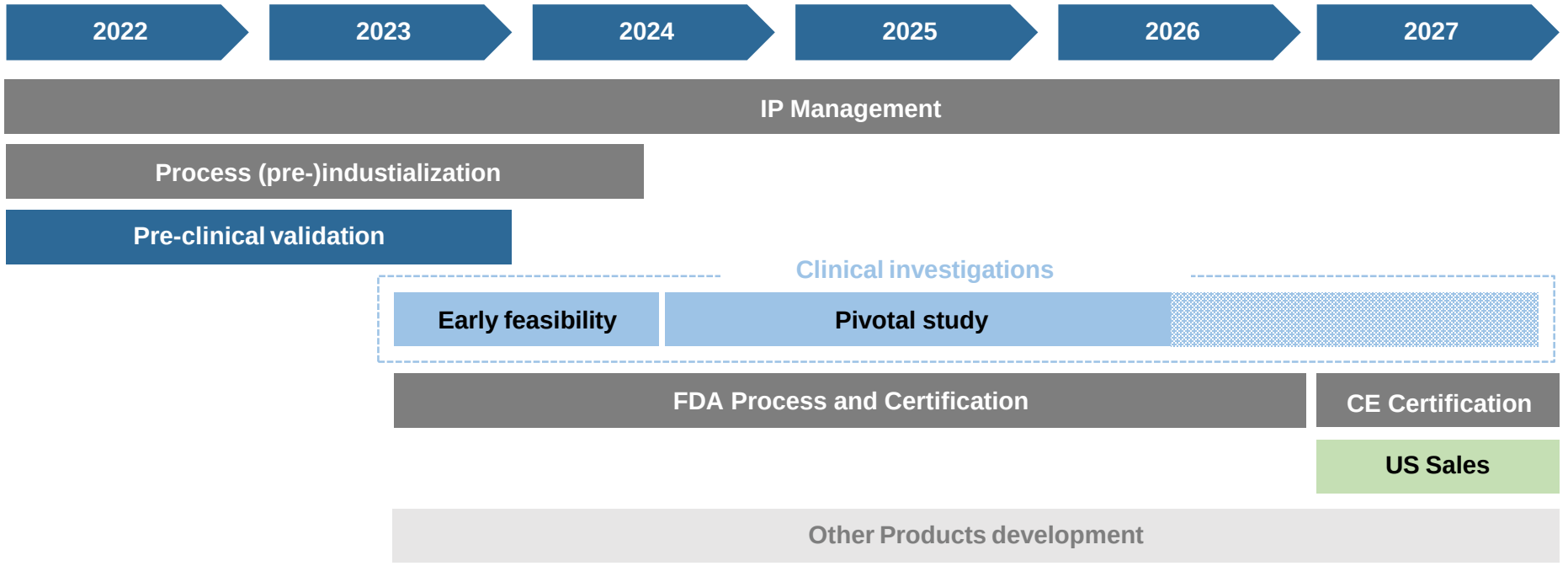
	Fistulae	Synthetic Arteriovenous grafts	CVC	Dialybrid
Long-term patency	✓	✗	✗	✓
Remodelling/integration	✓	✗	✗	✓
Resistance to infections	✓	✗	✗	✓
Availability	✗	✓	✓	✓
Early cannulation	✗	✓	✓	✓
Comfort for patients	✓	✓	✗	✓

Dialybrid is superior to alternatives along all dimensions considered

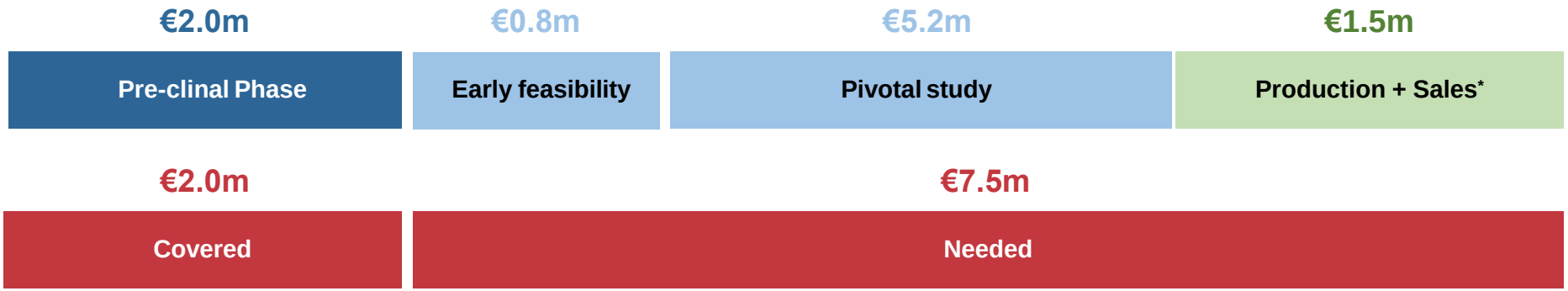
Table of Contents

Timeline for Marketability of Dialybrid AV Graft

DIALYBRID

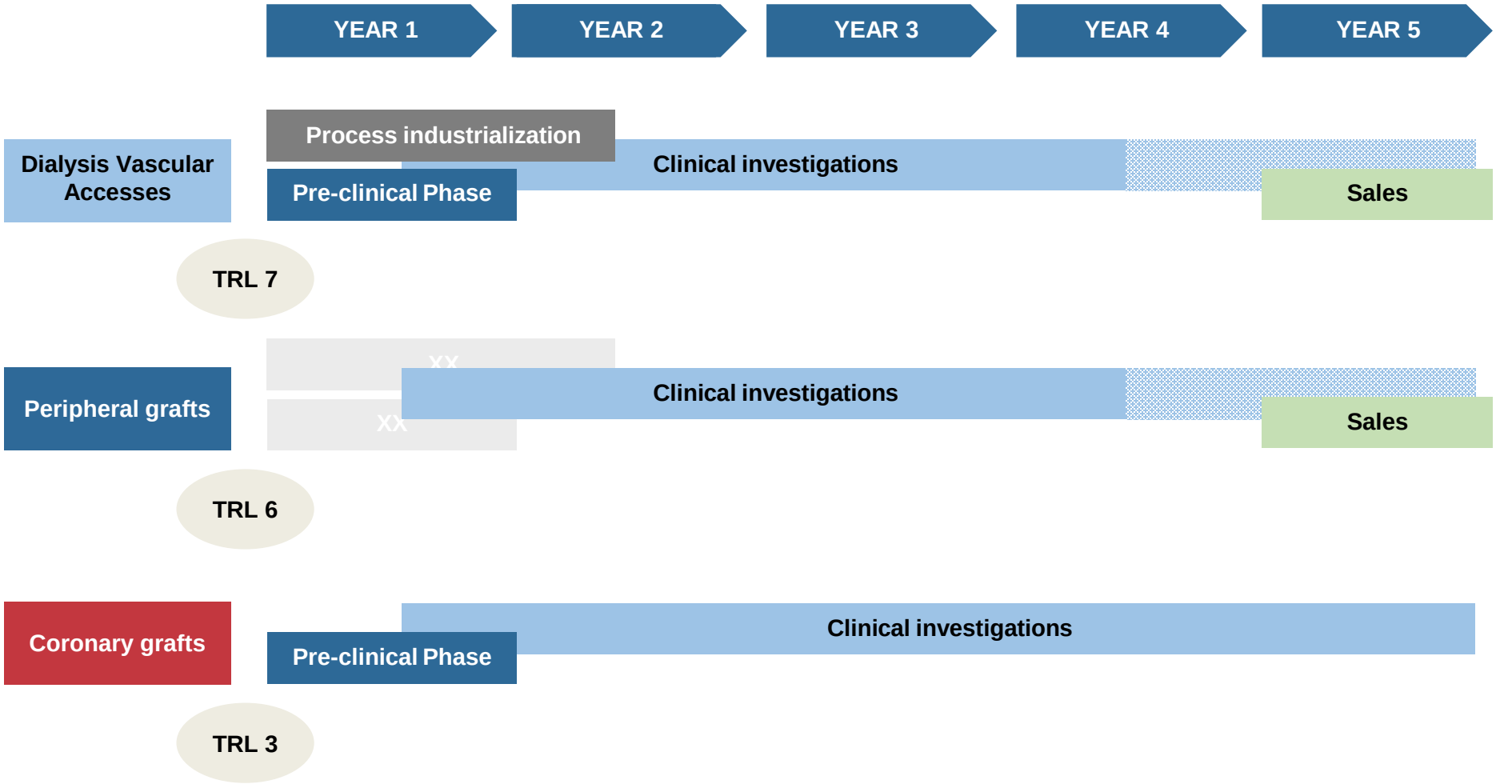


Funding Need for AV Graft Solution



Source: Company Information
Note (*): refers to an indirect distribution model

Parallel Opportunities



Dialybrid can capitalize on the pre-industrialization & preclinical phases of the AV graft saving time & expenditures to develop other products

Source: Company Information
Note (*): refers to an indirect distribution model

Total Funding Need

DIALYBRID

	Dialysis Vascular Accesses	Peripheral Grafts	Coronary Grafts
Investment needed	€9.5m	+ €5.0m	+ €9.0m
2025 Market Value	$1.2bn	$3.1bn	$7.9bn
Risk	↑ Low	↑↑ Medium	↑↑↑ High
2015-2025 CAGR	2.7%	11.6%	3.0%
	Current Focus		

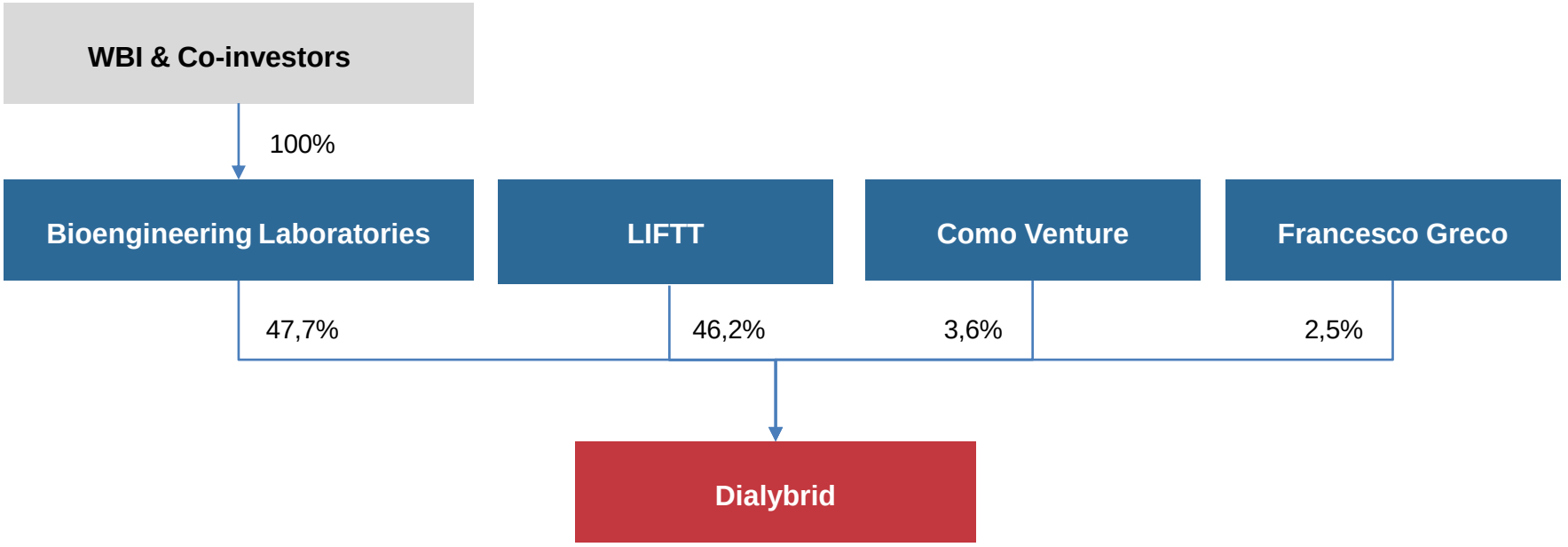
Dialybrid Ownership Structure

DIALYBRID

Closed rounds

	Round 1	Round 2	Round 3	Round 4	Total funding:
Date	*Jul-20*	*May-21*	*Feb-22*	*Giu-22*	**€1.950k**
Pre-money	€1.5m	€2.5m	€3.0m	€3.15m	
Investment	**€300k**	**€500k**	**€150k**	**€1.000k**	
Investor	LIFTT	LIFTT	Como Venture	LIFTT	

Current ownership



Source: Company Information

Table of Contents

Dialybrid had important contacts with the FDA

Interaction	Sending date	Feedback date	Main topics	FDA Feedback
Pre-Submission (main)	Mar 29th, 2021	Jun 9th, 2021	• Acuseal as predicate device? • Preclinical validation strategy (biocompatibility, animal study) • Clinical validation strategy • Suitability of 510(k)	▪ There is **no predicate device** ▪ Need to repeat the **animal study in GLP**, need of assessing **biostability** ▪ Too early to discuss clinical strategy ▪ **510(k) not a suitable route**
Supplement 1	Jul 27th, 2021	Oct 7th, 2021	• Design of GLP animal study • Design of a biostability study • Design of biocompatibility studies • Suitability of de novo 510(k)	▪ OK 12 animals for the **GLP study** ▪ Pre-approval of **biostability study**, requests on biostability of polyurethane ▪ OK on **Biological Evaluation Plan** ▪ **De novo 510(k) not a suitable route**
Supplement 2	Sep 3rd, 2021	Nov 9th, 2021	• Application for designation for Breakthrough Device Program (special “fast track” of FDA for breakthrough technologies)	▪ Application rejected due to the absence of clinical evidences of success ▪ Suggestion to collect preliminary clinical data (e.g., **feasibility study** on 10 subjects with 6 months follow up)
Supplement 3	Nov 22nd, 2021	Feb 4th, 2022	• GLP animal study protocol • Design of a biostability study on polyurethane • Non-clinical testing strategy table	▪ **GLP study** draft protocol approved ▪ Suggestions on how to improve the evaluation of the **biostability** of polyurethane (ISO 10993-13) ▪ Suggestions on the **preclinical tests**

Dialybrid is conducting the next pre-clinical phase

DIALYBRID

	Previous proof-of-concept animal study (@ UNIMI)			Future GLP animal study (@ Medanex, Belgium)		
Animal model	9 adult sheep, carotid-jugular arteriovenous shunt (deep)			12 adult sheep, carotid-jugular arteriovenous shunt (subcutis)		
Time-points	**MID-TERM** 1 month, 2 months, 3 months (N=3 per group)			**LONG-TERM** 1 month, 6 months, 12 months (N=4 per group)		
Certification	NONE			**GLP** (Good Laboratory Practice) ISO10993		
Study endpoints	Graft patency	100% patency rate @ 3 months	✓	Graft patency	To be evaluated via histo-pathology and echography	
	Graft remodeling	Endothelization @ 3 months	✓	Graft remodeling	Evaluated via histopathology and SEM analysis	
	Graft puncturability	Not assessed	✗	Graft puncturability	Assessed immediately after surgery & every 2 weeks	

Source: Riboldi SA et al., Adv Healthc Mater. 2020 Oct; 9(20): e2000794. doi: 10.1002/adhm.201200794

Table of Contents

Team

Francesco Giovanni Greco – CEO

- Mr Greco is an experienced medical devices entrepreneur, expert in bringing products from the lab to the market. He is a pioneer of medical engineering and co-inventor of around 20 patents
- Mr Greco holds a degree in Biomedical engineering

Stefania Adele Riboldi – Project Coordinator

- Mrs Riboldi is an expert in biomaterials and tissue engineering, management and coordination of research projects. She published more than 10 scientific papers and holds 2 patented applications
- She holds a PhD in Bioengineering

Alice Caldiroli – Product Development Engineer

- Mrs Caldiroli carried out her master's thesis work at Bioengineering Laboratories, focusing on the industrialization and validation of SAG
- She earned a MSc in Bioengineering at Politecnico di Milano

Cristina Oldani – Trainee, PhD candidate

- Mrs Oldani carried out her master's thesis at IIT in Genova, focusing on the degradative behavior of fibroin
- She earned a MSc in Bioengineering at Politecnico di Milano and she is currently a PhD student there

Teresa De Nadai – Project Manager LIFTT

- Mrs De Nadai is a neuroscientist of with a PhD in neurobiology
- She worked in the pharma industry for 4 years, as a coordinator of stability studies
- She is Project Manager at LIFTT since 2020, reference person of Dialybrid since its foundation

Source: Company Information

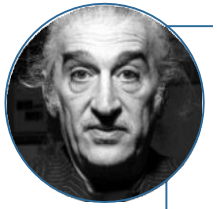
Consultants

Matteo Tozzi – Vascular Surgeon

- Associate professor of vascular surgery and Director of the Research Center for the Study and Application of New Technologies in Vascular Surgery at the University of Insubria

Franco Galli - Nephrologist

- Former Medical Director and Head of Vascular Access Surgery for Hemodialysis at the Division of Nephrology and Dialysis of the S. Maugeri Foundation in Pavia
- Consultant for medical device manufactures



Fabio Acocella – Veterinary Surgeon

- Associate Professor of Veterinary Surgery at Università degli Studi di Milano
- Study Director of SAG's first animal study
- Expert in animal models & study design in the fields of regenerative medicine, tissue engineering and gene therapy

Luciano Carbonari – Vascular Surgeon

- Head of the Vascular Surgery Unit at Ospedali Riuniti of Ancona
- Responsible for the regional center for vascular access in the Marche Region and collaborator of the study group of the Italian Society of Nephrology

Source: Company Information