

Hemoglobin Oxygen Therapeutics LLC

The world leader in life preserving oxygen carrying solutions

March 2021 Investor Presentation

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Mission Statement

To develop and commercialize the first and best in class technology platform for oxygen-carrying solutions addressing critical unmet medical needs in human and veterinary indications.



Company at a Glance

Delaware registered in 2014, technology is going back to 1990s with \$1 billion invested

\$20 million in equity financing to date

Acquired and developed the intellectual property for two Hemoglobin-Based Oxygen Carrier (HBOC) products :

- Hemopure (HBOC-201) for human use
- Oxyglobin (HBOC-301) for veterinary use

Existing collaborations in veterinary and human markets

Groundbreaking HBOC organ perfusion technology

Currently 12 employees

Production facility in Souderton, Pennsylvania

Highly experienced team

Zaf Zafirelis Co-Founder & CEO



30 years of Biotech, Pharma, and Medical Device industries More than 20 years CEO experience Raised more than \$100 million with successful exits

Joseph Rappold, MD Chief Medical Officer



30 years of active service (US Navy) with 6 combat deployments commanding a variety of medical facilities. Professor of Surgery at Tufts University. Chief of Acute Care Surgery and Trauma Medical Director at Maine Medical Center.

Greg Dube, PhD VP, Research & Development



30 years experience in drug R&D in large pharma and biotech firms.

Melissa Zafirelis

Director, Regulatory & Clinical Operations



Over 22 years multinational regulatory & clinical operations experience.

Igor Serov Co-Founder & CFO



Over 20 years of investment banking experience

Brian Dawson



25 years experience in development & commercialization of HbO2's products from pre-clinical research to product approval & marketing.

Arkadiy Pitman Senior Director, Statistics & Data Management



20 years of pharmaceutical & healthcare US experience with strong background in mathematics, statistics & logistics.

Fantao Meng

Director of Research and Development



Hemoglobin specialist with 20 years of research experience in developing hemoglobin-based oxygen carriers (HBOCs)



Hemopure and Oxyglobin

HBOCs with unique efficacy and safety profiles...

	Packed Red Blood Cells	Hemopure/Oxyglobin
STORAGE	Refrigerated	Room temperature (2-30°)
PREPARATION	Testing, typing, cross matching	Ready to use - no reconstitution
COMPATIBILITY	Type specific	Universal
SHELF-LIFE	42 days	36 months
PURITY	Tested and screened for known infectious agents	Sterile pharmaceutical product
	Blood, limited availability	Bovine hemoglobine : abundant, controlled source
EFFECTIVENESS	Dependant on storage length	Immediate oxygen delivery Same hemoglobin concentration as whole blood (13 g/dl)

Worldwide blood shortage

- Shortages of blood donations, not reaching the critical threshold of 30 per 1000 population in many countries
- COVID-19 pandemic highlights the need for a product that can successfully substitute blood's oxygen carrying capacity in time of need
- Hemopure has received marketing authorizations for acute anemia in South Africa & Russia



Therapeutics

Russia and South Africa alone cumulate a 3 millions blood units shortfall. Blood shortage represents a \$1 billion worldwide market per year.

Prehospital Trauma & Medical Readiness

- Strategic National Stockpiles
- Out-of-hospital / Ambulance services
- Remote locations / Military battlefield
 use



Therapeutics

Prehospital trauma (military & civilian) and disaster preparedness in the US markets represent \$500 million in revenue per year.

BNO Blood Is Not An Option

- Blood disorders including Sickle Cell disease, Hemolytic Anemia, etc.
- Rare blood types
- Religious objectors (refuse blood transfusion).



160,000 patients with blood disorders need transfusions per year in US and Europe, which represents \$400 million in revenue per year. Religious objectors represent another \$149 million in annual revenue in the United States alone.

Blood shortage, a similar issue in veterinary markets

- 2 million canine transfusions are needed annually in US and in Europe
- Veterinary product is approved in US and EU
- 30 different species has been successfully treated with Oxyglobin
- Only up to 25% of veterinary transfusion blood supplies are covered by blood banks
- 84% of US veterinarians are dissatisfied with current options

The US and European canine markets represent \$550 million in revenue.

HbO₂ Therapeutics

Organ Transplantation: Another Worldwide Shortage

- There is a constant demand for donated organs
- Organ eligibility criteria are extremely severe
- The ability to extend the life of organs ex-vivo and to assess their compatibility and health can dramatically improve the supply for transplantations
- The perfusion process allows doctors to assess reconditioning and viability of organs, limbs and tissues prior to transplantation both at room temperature and body temperature (37°C)

The transplantation market amounts to \$137 million per year.

→ Additional indications include...

- Ischemia indications including
 - ✓ Minimization of infarct size (STEMI ST-Elevation myocardial infarction)
 - ✓ Resuscitation from sudden cardiac arrest
 - ✓ Minimization of tissue loss in Limb ischemia / PAD claudication
- Antidote for carbon-monoxide and cyanide poisoning
- Oncology with solid tumors
- Burn victims and plastic surgery
- Perfusion of
 - ✓ Limbs prior to transplantation
 - ✔ Brain cells for diagnostic purposes

The average potential US market size in each of these new indications is \$500m.

Robust Pipeline

Product	Indication	Pre-Clinical	Proof of Concept	Pivotal	Approval	Marketing
Veterinary						
Oxyglobin	Anemia - Canine	\checkmark	\checkmark	\checkmark	\checkmark	\checkmark
Oxyglobin	Anemia - Felíne, Equine	\checkmark	\checkmark			Off-label use
Oxyglobin	Anemia - Zoological Species	\checkmark	\checkmark			Off-label use
Human						
Hemopure	Acute Anemia (S.Africa/Russia)	\checkmark	\checkmark	\checkmark	\checkmark	2022/23
Hemopure	Acute Anemia - Blood not an Option	\checkmark	\checkmark	\checkmark	2023 EU/US	
Hemopure	Acute Anemia - Pre-hospital Trauma	\checkmark	\checkmark	on-going	2023/24	
ZK1	Organ Perfusion for Transplantation	\checkmark	\checkmark	\checkmark	2022 EU	
ZK1	Limb / Flap Perfusion	\checkmark	\checkmark	2025		
HBOC-201	Smoke inhalation antidote	\checkmark	\checkmark	2022		
Hemopure	FDP reconstitution	\checkmark	\checkmark	2024/25		
HBOC-201	Solid tumor treatment	\checkmark	2021			
HBOC-201	Ischemia	\checkmark	\checkmark	2026		

Strong value creating recent progress

- •US Department of Defense signed and sponsored Hemopure trial for pre-hospital trauma
- Groningen liver transplantation trial finalized with 100% success
- Patent filed for HBOC/Freeze Dried Plasma combination
- Collaboration signed with Department of Defense and Teleflex on Hemopure use as a reconstitution agent for FDP
- Yale University brain perfusion study with Hemopure published in Nature
- Publication of high dose Hemopure case series
- Patent filed for smoke inhalation antidote
- Publication of an article supporting use of Hemopure in emergency preparedness including pandemics such as COVID-19

Strong value creating milestones

- FDA submission for Hemopure Phase 3 pivotal BNO clinical trial
- Start of hand transplant study
- Submission of the IDE for the kidney perfusion trial
- •Oncology collaboration for the treatment of refractory solid tumors
- Completion of production facility
- Filing of CE Mark for perfusion solution
- cGMP facility validation by US & EU regulators
- Oxyglobin market launch
- •Hemopure market launch in South Africa

Major academic & health centers collaborations

Expanded access program hospitals

UPPMC LIFE CHANGING MEDICINE

JOHNS HOPKINS BAYVIEW MEDICAL CENTER THE UNIVERSITY OF ILLINOIS AT CHICAGO

Over 300 peer-reviewed publications

Pretransplant seque	Arr ntial hypo- and normothermic machine	BATTER DAMAGNET BITMLIT DEPENDENT AND RAMPIN FOR	1991 2.17		CASE REPORT	Gright of Carlos Advance Liver	
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Characteristics of Hemopure

- Hb concentration 13 g/dL
- Plasma half-life ~ 19 hours
- Size = ~ 1 million < RBC
- Stable for 3 years at 2-30 °C
- Iso-osmotic, iso-oncotic
- P50 = 40 mm Hg
- Colloid (COP ~ to 6% albumin)
- Viscosity = 2.1 cP (~4 cP for RBC)

Relative Efficacy to Increase Total Hb

Impact of 250 mL : PRBCs > whole blood, > Hemopure, > hetastarch

HbO₂ Therapeutics

Vital Organ Blood Flow

- MAP responds to Hemopure; $\uparrow 10 20 \text{ mmHg}$
- Vital organ blood flow maintained

Tissue Oxygenation Vital Organ Oxygenation Maintained

• Hemodilution carried out in 3 stages: 10%, 30%, 50%

• Organ-specific tissue PO₂ determination via EPR imaging

Therapeutics

Expanded Access Real World Clinical Experience Representative Cases

Three sickle cell patients in crisis: RBCs refused/unavailable

- Hb nadirs 3.5 4.0 g/dL
- Febrile, MOF, neurologic dysfunction.
- Hemopure administered: 6, 23, and 27 Units
- Full recoveries

Kidney – Pancreas transplant: RBCs refused

- •Hb Nadir 2.0 g/dL
- •Tachycardia, tachypnea.
- •Hemopure administered: 12 units.
- •Full recovery

Autoimmune Hemolytic Anemia: RBCs refused

- Hb nadir 4.6 g/dL
- Elevated lactate
- Hemopure administered: 27 units.
- Full recovery

Ex-situ Perfusion prior to Transplantation

Transplantation of high-risk donor livers after ex situ resuscitation and assessment using combined hypo- and normothermic machine perfusion: a prospective clinical trial

Declined livers (ECD = high-risk)

DHOPE = dual hypothermic oxygenated machine perfusion (4°C - 12°C).

- COR = controlled oxygenated rewarming.
- NMP = normothermic machine perfusion $(37^{\circ}C)$

Post-operative results

- 12-mo Graft survival: 100% (\geq std DCD & DBD)
- Peak ALT & AST: << std DBD & DCD
- DHOP-COR-NMP: ↑ donor livers 20% vs. std DCD & DBD

Machine Perfusion (minutes)

Van Leeuwen et al, Ann Surg, 2019 de Vries Y, et al. BMJ Open 2019

Manufacturing capacities

The manufacturing process involves two stages:

Sourcing of bovine blood Stage I

Second stage of purification Stage II

- Facility building is fully constructed
- Stage I is in place and operational (\$20m replacement value)
- Stage II all equipment is acquired and waiting for installation (\$70m replacement value)
- Production facility fully operational in 9 months
- Expansion capacity is secured on an adjacent plot

Certification from US and EU regulators is expected in 18 months

Extraction of hemoglobin

Polymerization

Therapeutics

Hemopure

Cash positive in 2023 with \$50m investment \$20m commitment secured

Year	2022 \$m	2023 \$m	2024 \$m	2025 \$m	2026 \$m	2027 \$m
Total Revenues	0.8	26.9	50.9	118.4	157.5	211
EBITDA	-16.6	8.9	29.1	93.4	125.3	168.9
Free Cash-Flow	-26.9	4.8	25.0	68.8	93.5	94.2

Why invest in HBO2?

Strengths	 Innovative products with superior competitive advantages Highly experienced team Existing approvals in both animal and human markets Distribution agreement for veterinary market Near term profitability and net cash flow
Opportunities	 Cash efficient plan to achieve market approvals and products launches Multi-billion dollar potential markets Potential additional indications Easy expansion into new geographical areas