QOOL Therapeutics

Novel Therapeutic Hypothermia Technology

Amir Belson, MD
Qool Therapeutics Mission

Qool Therapeutics is dedicated to creating non-invasive, efficient temperature management therapies to preserve cells, and improve both quality and length of life.

Qooling saves hearts and minds.
Therapeutic Hypothermia (TH)
Temperature range is 32-35° Centigrade

- Gold standard treatment for reperfusion injury
- Therapeutic hypothermia is
  - Pluripotent
    - Slows inflammation, cell damage and reduces cell oxygen requirements
  - Standard of care for cardiac arrest
    - Two NEJM pivotal studies; American Heart Association Guidelines
  - Used as neuro-protective adjunct in neurosurgery, AAA, and bypass surgery
  - Emerging treatment for acute coronary syndromes

“More potent than antibiotics” – Gary Steinberg, M.D., Ph.D.
Chairman, Department of Neurosurgery, Stanford University
Current Therapies Fall Short

Unmet Need for Non-Invasive, Efficient Cooling Easily Compatible with the Flow of Patient Care

Non-invasive Products
- Cooling pad/blankets
- Inefficient; time to target temperature = 4-6 hours

Invasive Products
- Cooling catheters
- More efficient cooling; disruption in flow of care & complications

Patient Care

Vs.
Qool Therapeutics, The Solution

Qool Therapeutics' frozen, aerosolized saline system utilizes the efficiency of the lungs to cool the body similar to the way a radiator cools your car.
Qool Therapeutics Formula

• Exploit the large surface area of the lungs and direct blood path to the heart and brain

• Exploit the latent heat of frozen saline (H\textsubscript{2}O)
  • Frozen saline at 0\textdegree{} C contains eight times the cooling capacity of liquid saline at 0\textdegree{} C
  • Saline used because of its pH and osmotic pressure levels
    • Will not harm lung tissue and is easily absorbed

• Develop small portable disposable frozen saline aerosol delivery package
  • Few milliliters of saline per breath over short induction phase needed to reach and maintain therapeutic levels of hypothermia
    • Studies show that the lungs can easily absorb this quantity
Total Available Market – US and Europe
5 Million Patients Affected, $5 Billion+ Market Opportunity

Disease Management

- ST segment elevation MI (STEMI)¹
- Post sudden cardiac arrest (after ROSC)²
- Stroke³
- Traumatic brain Injury⁴
- Acute spinal cord injury⁵
- Hyper metabolic diseases (sepsis, burns, heat stroke)⁶
- Status Epilepticus⁹

Total = 4.65 million patients affected

Adjunct to Surgery - Protective Therapy

- Cardiac surgery - surgical valve repair and off pump cardiac bypass⁷
- Peripheral vascular surgery - carotid endarterectomy and stent placement, neurovascular surgery⁸

Total = 690,000 patients affected

Data sources for footnotes 1 through 9 included at end of the presentation
Therapeutic Hypothermia - Use in the Military Sector

**Battlefield**
- Exercise/exertion recovery
- Trauma
- Traumatic brain injury
- Acute spinal cord injury
- Hyper metabolic diseases – heat stroke, sepsis
- Burns and smoke inhalation injury

**Surgery**
- Protective effect in
  - Neurosurgery
  - AAA surgery
  - Peripheral vascular surgery
Exercise Recovery - Expansion Market Opportunity
Consumer Use with Potential for Early Concussion Treatment

Tier I - Over 400 Professional Teams, ~9000 Professional Athletes
Tiers II and III, Over 1.2 Million College and High School Athletes

Tier I
- US Professional Leagues
- Global Cycling & European Soccer

Tier II
- NCAA Division I College Athletic Programs

Tier III
- NCAA Division II/III College, & High School Athletic Programs
Qool Therapeutics Compares Favorably to Competitors
Non-invasive, Efficient Cooling, Easily Integrated into the Flow of Care

Qool Therapeutics
PneumoQool

Others (localized cooling, target organ):

Cryothermic Systems (brain)
CoolSpine (spine)
QuickCool AB (brain)
ThermopeutiX (brain)
TraumaTec (brain)
Neurosave (brain)

In Development:
Advanced Cooling Therapy – Esophageal Cooling Device
Progress on Key Milestones
Successfully completed

- Prototype frozen saline generation machine
- Prototype frozen saline delivery machine & patient interface delivery tube (ET Tube)
- Prototype reservoir mask for frozen delivery in a conscious patient
- Physiologic bench test models
- Cooling in all acute porcine animal studies with dose response demonstrated

  - Faster cooling with increased frozen saline delivery/inhaled breath
  - No gross evidence of insult to the animals’ respiratory system
Acute Porcine Animal Study Results - Summary

• No major untoward physiologic effects seen in these studies
• Core and total body cooling achieved
• Faster cooling than any competitor
  – Fastest cooling achieved = 0.41°C/minute, 7X faster than cooling catheters, 41X faster than infused saline or cooling blankets
• Core/central temperature reduction of 2°C in less than 20 minutes of cooling time demonstrated in multiple animal studies (descending aorta temperature)
• Dose response demonstrated
  – System flexibility allows for induction, maintenance and re-warming phases; range of cooling regimens
Animal Study Example 1

Porcine Study Demonstrates 3°C Temperature Reduction
Continuous Cooling, Maintenance and Re-warming Demonstrated

*Cooling Induction*
- Temp Decrease: 3°C in Descending Aorta and Jugular in 97.7 min
- Cooling Rate: 0.032°C/min
- Delivery Rate: 18.2 g/min

*Temperature Maintenance*
- Jugular Temp controlled to 33.9°C ± 0.1 for 30 minutes
- Delivery Rate: ~5 g/min

*Passive Rewarming*
- 16 min duration
- No Delivery
Animal Study Example 2

Fast, Continuous Cooling, Maintenance and Re-warming Demonstrated

Temperature Reduction: 2°C in 17 min.; 3°C in 42 min.

- Cooling Induction
  - Temp Decrease: 3°C in Descending Aorta in 41.9 min
  - Cooling Rate: 0.072°C/min
  - Delivery Rate: 24.1 g/min

- Temperature Maintenance
  - Jugular Temp controlled to 34.5°C +/- 0.1 for 30 minutes
  - Delivery Rate: ~8 g/min

- Passive Rewarming
  - 30 min duration
  - No Delivery

- Descending Aorta
- Inferior Vena Cava
- Jugular
- Rectal
- Tympanic

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Animal Study Example 3

Fast, Continuous Cooling, Maintenance and Re-warming Demonstrated

Temperature Reduction: 2°C in 19 min.; 3°C in 39 min.
Summary

• A novel non invasive technology to extend the “golden hour”.
• Faster than any other technology
• Enables well controlled maintenance and rewarming
• Applicable in multiple medical conditions