VITAL THERAPIES®

TARGETING LIVER DISEASE

Vital Therapies, Inc. (VTL:NASDAQ)

Corporate Introduction

May 2017

Forward Looking Statements

This presentation contains forward-looking statements. All statements other than statements of historical facts contained in this presentation are forward-looking statements, including, among others, statements relating to plans and objectives of management for future operations and future results; pre-specified and post-hoc analyses of VTI-208 data; the timeline for future operations, including VTL-308; the design of VTL-308, including inclusion and exclusion criteria, the timing for the enrollment, and the timing for the release of data; hypotheses relating to the ELAD® system's mechanisms of action; market opportunity and size; reimbursement matters and pricing of the ELAD System; and timing for regulatory filings. These statements involve known and unknown risks, uncertainties and other important factors that may cause our actual results, performance or achievements to be materially different from any future results, performance or achievements expressed or implied by the forward-looking statements. Risks and uncertainties include, but are not limited to the uncertainties inherent in our clinical and development programs, including, without limitation, our ability to adequately demonstrate the safety and efficacy of the ELAD System, clinical results, which may not support further development of the ELAD System, and challenges related to conducting pivotal clinical trials, including, but not limited to, the impact of VTI-208, failure to achieve favorable results in clinical trials, the participation of clinical sites and their ongoing adherence to protocols, assumptions regarding enrollment rates, timing and availability of subjects meeting inclusion criteria, changes to protocols or regulatory requirements, the ability to comply with and meet applicable laws and regulations, and unexpected adverse events or safety issues; the ability to obtain regulatory approval for the ELAD System; and the sufficiency of funding. There can be no assurance that data from any of our clinical trials will be sufficient to support an application for marketing in any country or that any such application will ever be approved.

You should review the risks and uncertainties contained in our filings with the United States Securities and Exchange Commission, including risks and uncertainties described in detail under the caption "Risk Factors" in such filings. Because forward-looking statements are inherently subject to risks and uncertainties, some of which cannot be predicted or quantified and some of which are beyond our control, you should not rely on these forward-looking statements as predictions of future events. The events and circumstances reflected in our forward-looking statements may not be achieved or occur and actual results could differ materially from those projected in the forward-looking statements. All statements made in this presentation speak only as of May 9, 2017. Except as required by applicable law, we do not plan to publicly update or revise any forward-looking statements contained herein, whether as a result of any new information, future events, changed circumstances or otherwise.

VTL: Focused on Saving Lives

80,000 people suffer from acute forms of liver failure each year in the US and Europe with up to 50% mortality

Our goal is to save their lives

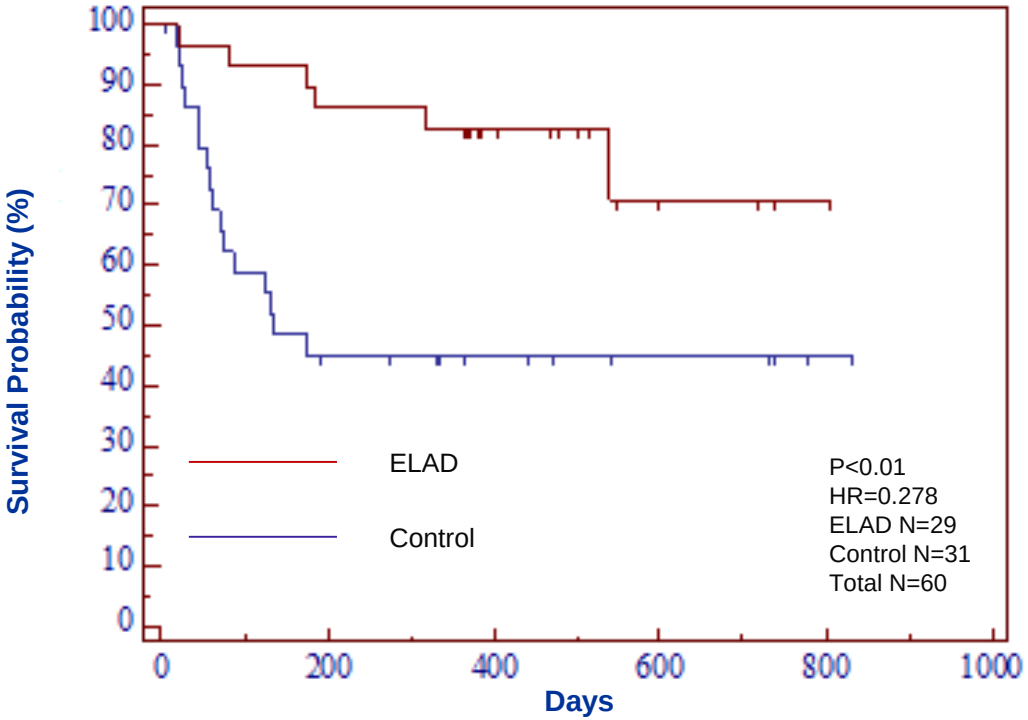
Our technology seeks to use the power of human liver-derived cells to promote liver recovery

Phase 3 trial underway driven by large clinical data set from prior trial with topline results expected around mid-2018

A multi-billion orphan market opportunity where transplant is generally not available

VTL: Current Focus is VTL-308 Trial

Ongoing Phase 3 clinical trial in the US and EU seeking to confirm the findings of prior clinical trial (VTI-208) conducted in severe Alcoholic Hepatitis (sAH). Target population: younger subjects without evidence of multi-organ failure. Overall survival based on post-hoc analysis (combination of pre-specified parameters) of VTI-208 trial is as follows:



Management & Board: Proven Record of Success

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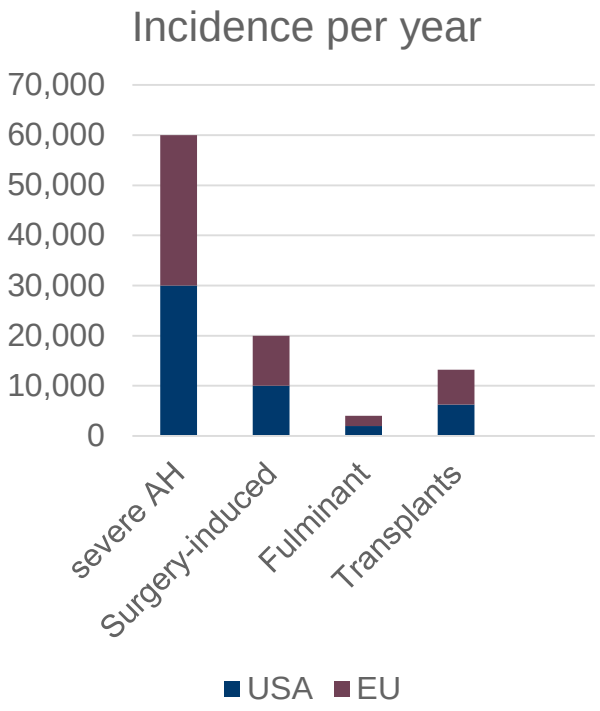
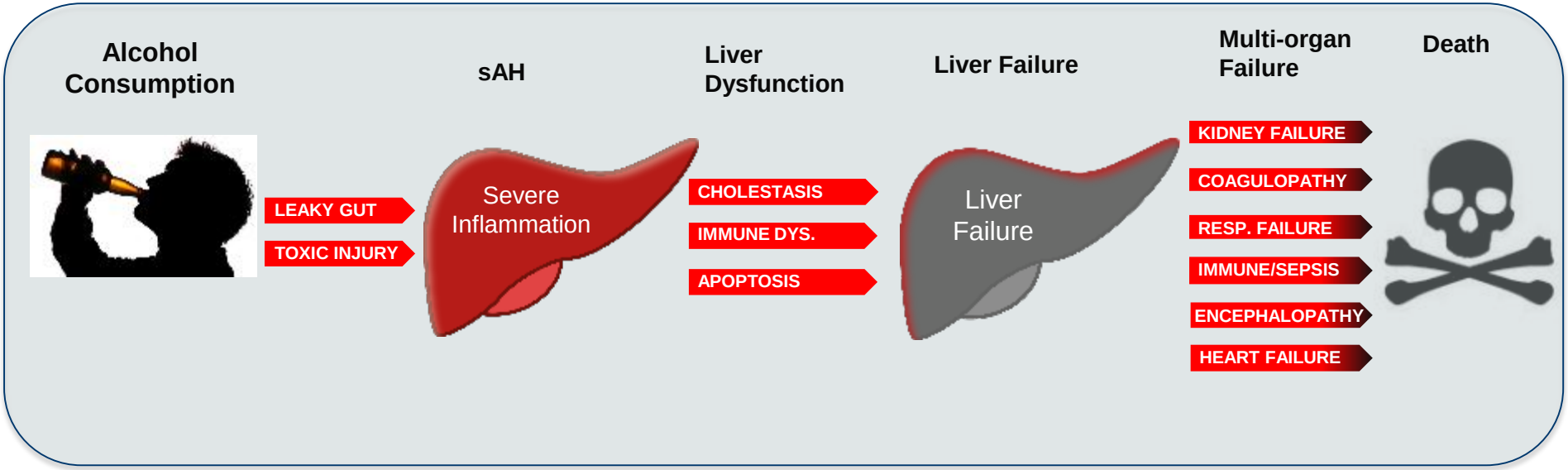
Acute Forms of Liver Failure Have High Mortality

- Life-threatening crises
  - But liver can regenerate to complete recovery
- Transplant is only therapy proven to increase survival
  - Severely limited by cost and donor availability
  - >90% adult transplants are in chronic patients
- Severe Alcoholic Hepatitis (sAH) is lead clinical target:
  - Rapid onset of jaundice and liver failure caused by binge drinking
    - Inflammatory disease of the liver
    - Very different from cirrhosis (scar formation)
  - About 50% mortality



Severe Alcoholic Hepatitis (sAH)

- Associated with binge drinking
- Severe liver inflammation
  - Swelling leading to obstruction of bile flow and jaundice
  - Increased oxidative stress
  - Decreased hepatocyte function
- Can progress through increasing morbidity to death



Recovery from sAH is Possible

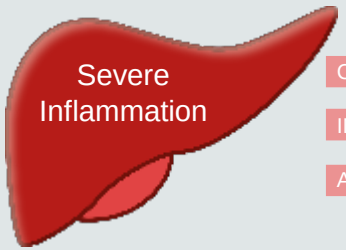
Stabilization

- REDUCE INFLAMMATION
- PROMOTE CELL SURVIVAL/REGENERATION
- IMPROVE HOMEOSTASIS/ IMMUNE FUNCTION
- IMPROVE BILE FLOW
- PROVIDE METABOLIC SUPPORT

Alcohol Consumption

- LEAKY GUT
- TOXIC INJURY

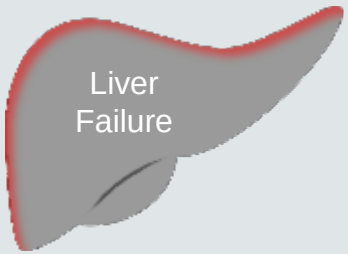
sAH



Liver Dysfunction

- CHOLESTASIS
- IMMUNE DYS.
- APOPTOSIS

Liver Failure



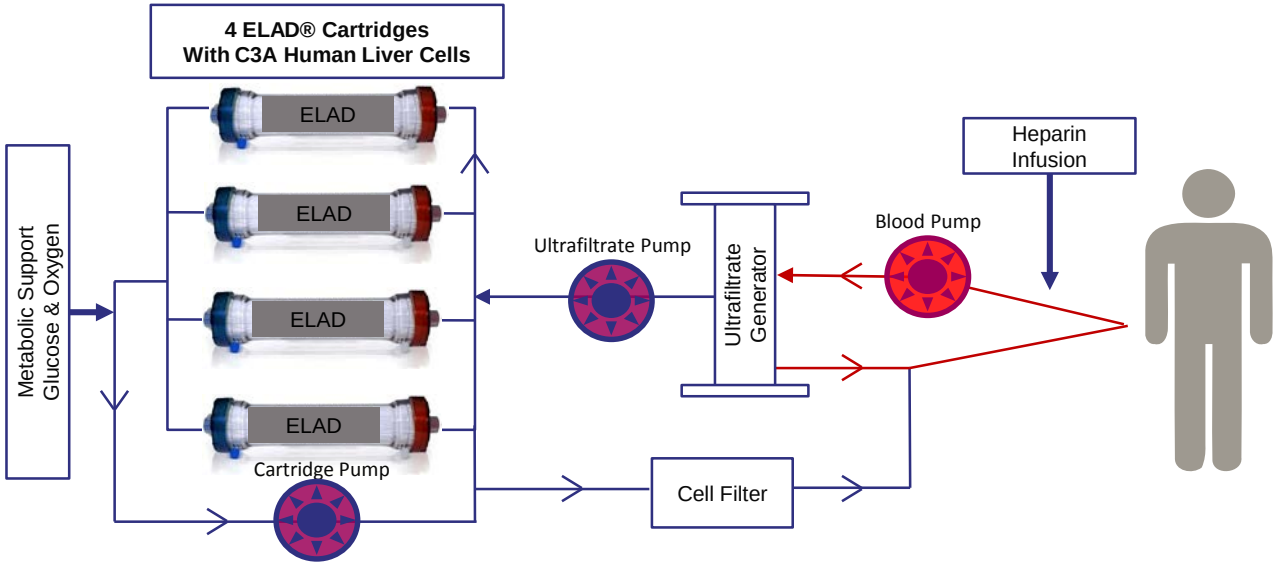
Multi-organ Failure

- KIDNEY FAILURE
- COAGULOPATHY
- RESP. FAILURE
- IMMUNE/SEPSIS
- ENCEPHALOPATHY
- HEART FAILURE

Death

The ELAD® System: Human-cell Bio-Artificial Liver

- **Bio-artificial liver system designed to improve survival in acute forms of liver failure**
  - Several hundred billion liver-derived cells (about one pound of cells)
  - Continuous treatment for 5 days



- **Allogeneic <u>cellular therapy</u> based on VTL C3A cells**
  - Human — No animal safety issues with the cells
  - Scalable — Can be grown in large quantities
  - Proprietary — VTL owns cell banks

ELAD Uses Human Liver-derived Cells to Support Liver Function

- **VTL C3A cells produce a variety of proteins that carry out functions critical to life**

Reduce inflammation

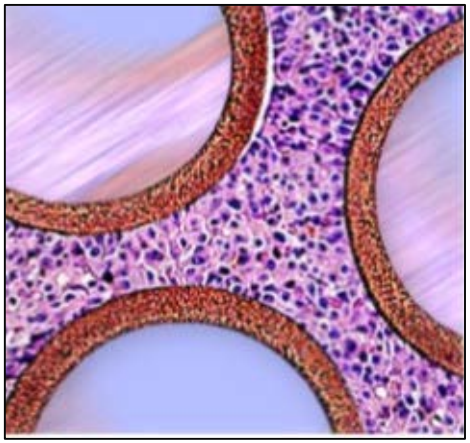
- Alpha-1-Antitrypsin
- Complement C3
- Ferritin
- Gelsolin
- Haptoglobin
- Intercellular Adhesion Molecule 1
- Interleukin-1 Receptor Antagonist
- Interleukin-8

Promote Cell Survival/Regeneration

- Amphiregulin
- Heparin-Binding EGF-like Growth Factor
- Hepatocyte Growth Factor
- Platelet-Derived Growth Factor-BB
- Tissue Inhibitor of Metalloproteinases 1
- Tissue Inhibitor of Metalloproteinases 2
- Tissue Inhibitor of Metalloproteinases 3
- Transforming Growth Factor Alpha
- Growth/differentiation factor 15 (GDF-15)
- Heat-Shock protein 70 (HSP-70)

Improve Homeostasis / Immune Function

- Albumin
- Transferrin
- Reduce IL-1β secretion in macrophages



Improve Bile Flow

- Decrease conjugated primary bile acids
- Increase secondary conjugated bile acids
- Reduce circulating bilirubin

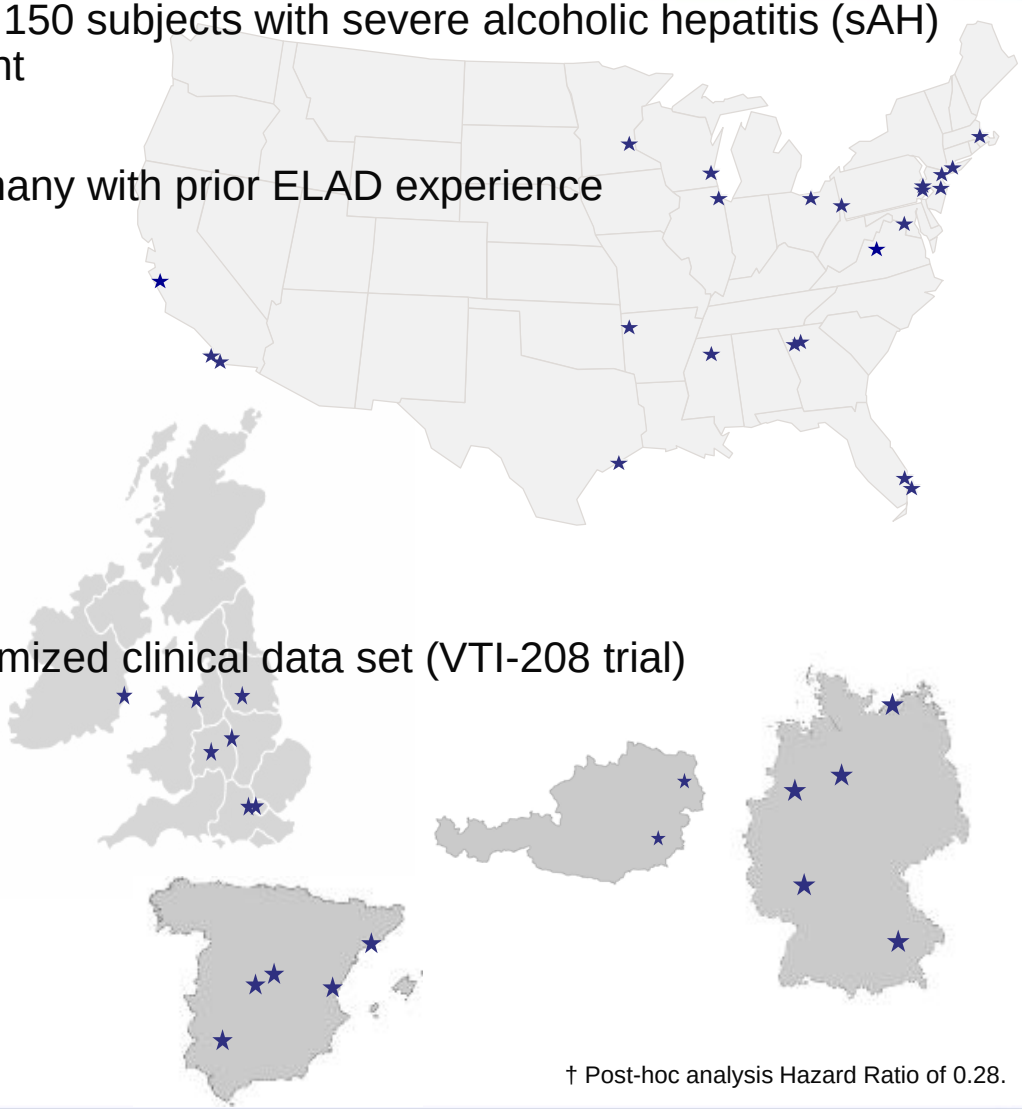
Provide Metabolic Support

- Peroxiredoxin-4 (Prx-IV)
- Fatty Acid-Binding Protein (FABP), liver
- Creatine phosphate
- Provide Cytochrome P-450 activity
- Improve amino acid metabolism

*Proteins may have multiple roles depending on concentration and targeted cell type. MOA theories are based on laboratory studies and need correlation with in vivo studies and patient outcomes.

Pivotal VTL-308 Trial Underway

- Randomized, controlled trial in at least 150 subjects with severe alcoholic hepatitis (sAH) with overall survival as primary endpoint
- Target of 50 sites in US and Europe, many with prior ELAD experience
- Timeline:
  - FDA written guidance received Q4:2015
  - First subject enrolled in Q2:2016;
  - **67 subjects enrolled as of May 8, 2017**
  - Topline data expected around mid-2018
- VTL-308 criteria guided by large randomized clinical data set (VTI-208 trial)
- Powering at various hazard ratios:
  - ~ 99% for 0.30 †
  - > 95% for 0.40
  - > 85% for 0.50



† Post-hoc analysis Hazard Ratio of 0.28.

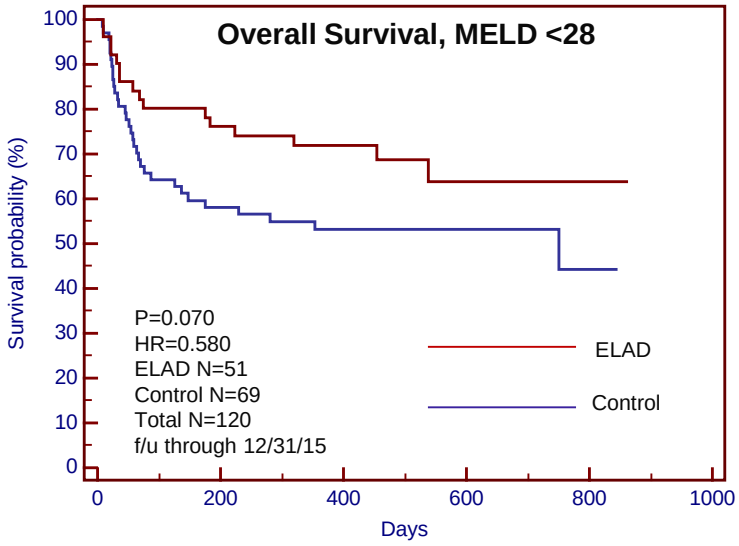
Large Data Set from Prior Trial Drives VTL-308

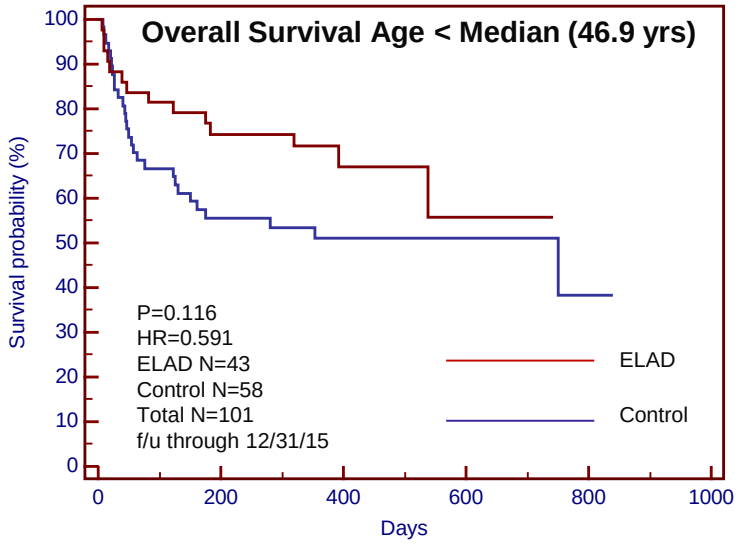
VTI-208 – 1:1 randomized, controlled data set with 203 subjects followed up to 800 days

- Did not reach primary endpoint in ITT population
- Trend to improved survival in less advanced and younger subjects

91 day survival – Pre-specified parameters:	ELAD Survival	Control Survival	Relative Improvement	Absolute Improvement	P value*	N
MELD<28	80.4%	65.2%	23.3%	15.2%	0.068	120
Younger (under 46.9)	81.4%	67.2%	21.1%	14.2%	0.112	101

* Pearson's chi-squared test, ELAD vs. Control





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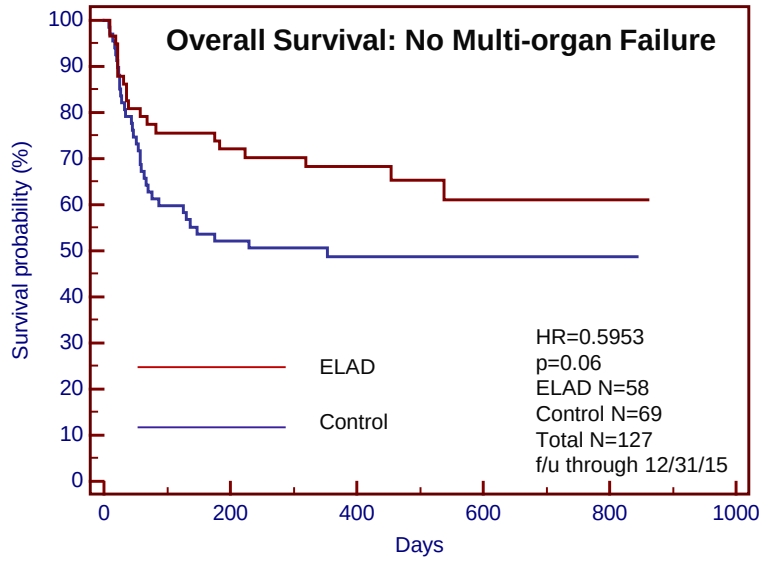
Large Data Set from Prior Trial Drives VTL-308

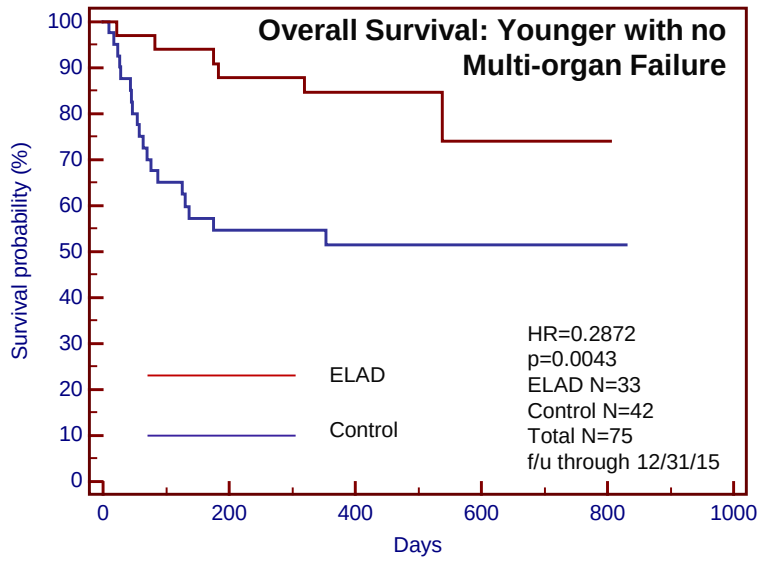
VTI-208 – 1:1 randomized, controlled data set with 203 subjects followed up to 800 days

- Trend in improved survival in younger subjects with no multi-organ failure

91 day survival – Combination of Pre-specified parameters	ELAD Survival	Control Survival	Relative Improvement	Absolute Improvement	P value*	N
No multi-organ failure (Creatinine<1.3 mg/dL, INR≤2.5)	75.9%	60.9%	24.6%	15.0%	0.072	127
Younger with no multi-organ failure (Age<50, creatinine<1.3 mg/dL, INR≤2.5)	93.9%	66.7%	40.8%	27.2%	0.004	75

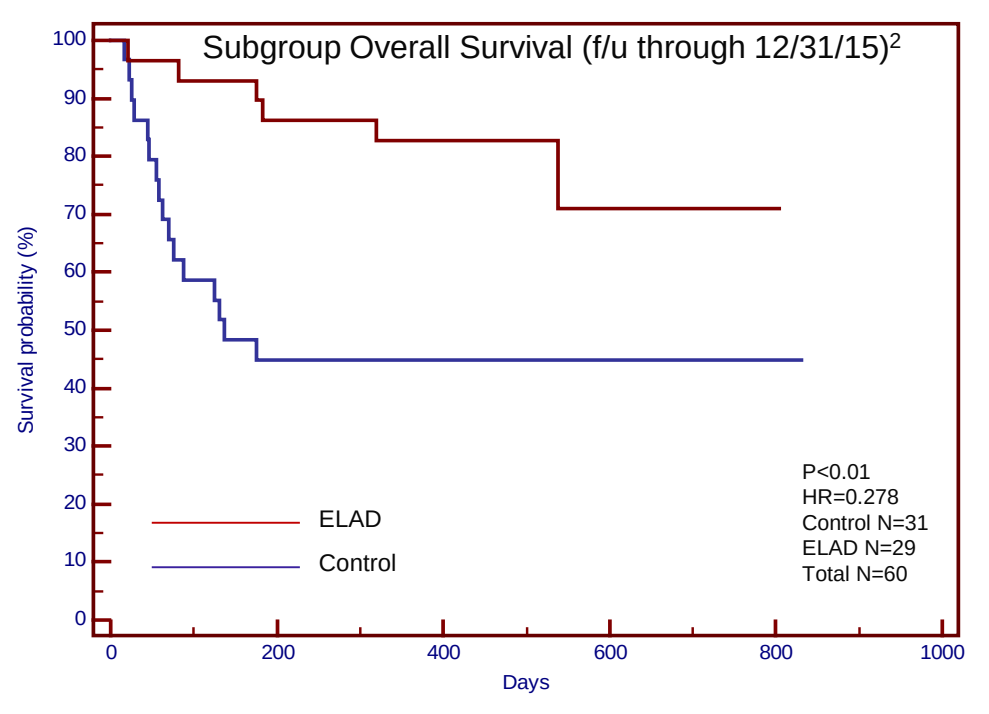
* Pearson's chi-squared test, ELAD vs. Control





Phase 3 Trial Targets sAH with No Other Organ Failures

VTI-208 Subgroup: Age <50; INR ≤2.5; creatinine <1.3 mg/dL; and bilirubin ≥16 mg/dL[1]



Baseline	ELAD Treatment (N=29)	Control (N=31)
Age	39.6±5.07	40.5±6.38
MELD	25.3±2.18	25.8±2.08
Creatinine	0.66±0.23	0.75±0.27
Bilirubin	26.6±7.2	26.7±5.6
INR	1.84±0.36	1.88±0.30
Sodium	133.1±5.6	133.7±4.2

60 subjects with hazard ratio of 0.28; p < 0.01

- 91-day survival: **ELAD 93% versus Control 61%**
- 180-day survival: **ELAD 89% versus Control 48%**
- 365-day survival: **ELAD 82% versus Control 41%**[3]

[1] Bilirubin minimum added to increase mortality in both ELAD and control arms.

[2] There were no transplants in this subgroup.

[3] Excludes from calculation 1 ELAD-treated subject and 4 control subjects who had not reached 365 days as of 12/31/15.

Sizeable Orphan Market

- Approximately 80,000 patients per year across US and EU

	Severe Alcoholic Hepatitis	Fulminant Hepatic Failure	Surgery-induced Acute Liver Failure	TOTAL
United States	30,000 validated	2,000 validated	*10,000+ estimated*	40,000+
Europe†	*30,000+ estimated*	*2,000+ estimated*	*10,000+ estimated*	40,000+

- sAH is lead indication, but potential addressable market includes all acute and sub-acute forms of liver failure

† *Estimated based on US data and relative population sizes.*

Blockbuster Opportunity

- Expert consultant (MME) recommended price range from $150 to $275K for ELAD:
  - Substantial pricing precedence with orphan therapies

Product	Company	Approval		Indication	US Disease Prev	US Annual WAC	EU Annual ex-Factory Price Range
		FDA	EMA				
Soliris	Alexion	2007	2007	PNH	4,000	$444K[2]	$345K to 482K[2]
Cinryze	ViroPharma	2008	2011	HAE	6K to 10K	$392K[2]	$171K to 334K[2]
Carbaglu	Orphan Europe	2010	2003	NAGS deficiency	300	$635K[1]	$373K to 497K[1]
Kalydeco	Vertex	2012	2012	CF	30,000	$297K[2]	$238K to $349K
Juxtapid	Aegerion	2012	N/A	HoFH	300	$235-$295K[2]	N/A
Gattex	NPS	2012	N/A	Short Bowel Syndrome	10K – 20K	$284K[2]	N/A

1. 25kg patient; 2. Fixed dose

- Compelling value proposition:
  - Penetration of 20-30% suggests multi-billion dollar market opportunity
    - If VTL-308 is successful, ELAD will have shown durable improvement in overall survival
    - In a market that is concentrated and lacks competition
  - Anticipate attractive gross margins at commercial volume and a modest sales force targeting up to 200 centers in each of the US and EU
  - Could it become a frontline therapy and standard of care?

ROW Also Presents Large Opportunity

- ELAD market in ROW anticipated to focus on future indications:
  - Acute flares of hepatitis B (see VTIC-301 for clinical data)
  - Supporting resections of liver cancer (anecdotal evidence from compassionate use; formal trial would likely be required)
- Large patient populations highlight the significant need and even a small % of ROW represents a multi-billion dollar opportunity
  - ELAD may be an effective therapy in subgroups of these populations:

	Hepatitis B	Liver Cancer
China	130M (estimated to result in 2M acute hepatocellular dysfunction/liver failure cases per year)	395,000
India	40M+	27,000
Russia	2-7% of pop. (~3-10M)	7,000
Brazil	2% of pop. (~4M)	10,000
Middle East	2-5% of pop. (~8-19M)	25,000
Japan	2% of pop. (~2.5M)	36,000
Worldwide	2B have been infected in lifetime. 10 - 50 million new cases per year 350-400 million chronic carriers; 75% in Asia	750,000 new cases/yr 6th most common cancer 3rd leading cause of cancer death

Intellectual Property and Exclusivity

Patent Protection

- Key U.S. Patent Issued in 2012, term to April 2027
  - Covers use of the C3A cell-line in ELAD System to treat liver failure
- December 2013 patent covers bedside unit; term to May 2025
- Other patents granted and pending in US and around the world

Orphan Designation

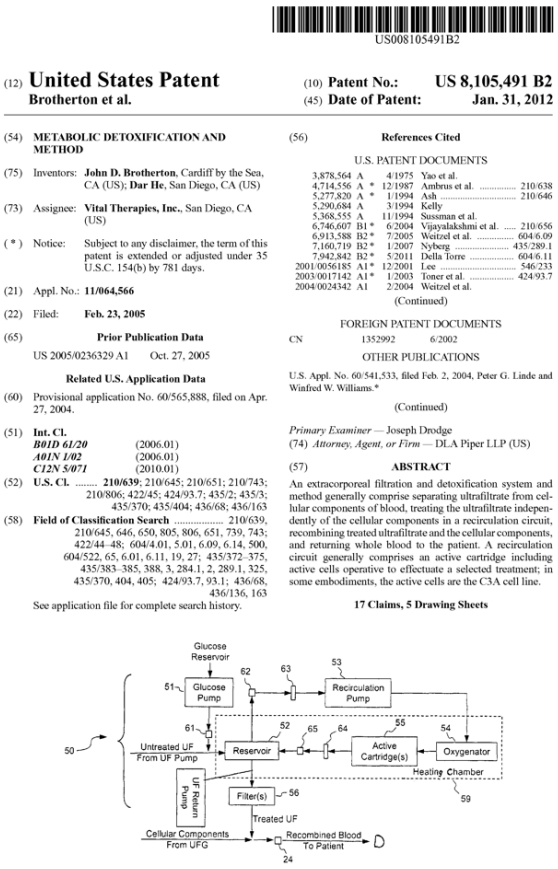
- Granted by FDA and EMA for treatment of acute liver failure
- Provides 7 years of market exclusivity upon FDA approval; 10 years in EU

Biologics Price Competition and Innovation Act

- 12 years of data exclusivity upon FDA approval
- Keeps bio-similars off the market during exclusivity period

Trade Secrets

- Maintaining and growing C3A cells is very difficult
- Know-how is held as trade secrets



US008105491B2

(12) **United States Patent**
Brotherton et al.

(10) **Patent No.: US 8,105,491 B2**
(45) **Date of Patent: Jan. 31, 2012**

(54) **METABOLIC DETOXIFICATION AND METHOD**

(75) Inventors: **John D. Brotherton**, Cardiff by the Sea, CA (US); **Dar He**, San Diego, CA (US)

(73) Assignee: **Vital Therapies, Inc.**, San Diego, CA (US)

(*) Notice: Subject to any disclaimer, the term of this patent is extended or adjusted under 35 U.S.C. 154(b) by 781 days.

(21) Appl. No.: **11/064,566**

(22) Filed: **Feb. 23, 2005**

(65) **Prior Publication Data**

US 2005/0236329 A1 Oct. 27, 2005

Related U.S. Application Data

(60) Provisional application No. 60/565,888, filed on Apr. 27, 2004.

(51) **Int. Cl.**
B01D 61/20 (2006.01)
A01N 1/02 (2006.01)
C12N 5/071 (2010.01)

(52) **U.S. Cl.** **210/639**; 210/645; 210/651; 210/743; 210/806; 422/45; 424/93.7; 435/2; 435/3; 435/370; 435/404; 436/68; 436/163

(58) **Field of Classification Search** 210/639, 210/645, 646, 650, 805, 806, 651, 739, 743; 422/44–48; 604/4.01, 5.01, 6.09, 6.14, 500, 604/522, 65, 6.01, 6.11, 19, 27; 435/372–375, 435/383–385, 388, 3, 284.1, 2, 289.1, 325, 435/370, 404, 405; 424/93.7, 93.1; 436/68, 436/136, 163

See application file for complete search history.

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(Continued)

Primary Examiner — Joseph Drodge
(74) *Attorney, Agent, or Firm* — DLA Piper LLP (US)

(57) **ABSTRACT**

An extracorporeal filtration and detoxification system and method generally comprise separating ultrafiltrate from cellular components of blood, treating the ultrafiltrate independently of the cellular components in a recirculation circuit, recombining treated ultrafiltrate and the cellular components, and returning whole blood to the patient. A recirculation circuit generally comprises an active cartridge including active cells operative to effectuate a selected treatment; in some embodiments, the active cells are the C3A cell line.

17 Claims, 5 Drawing Sheets

VITAL THERAPIES®

Cash Position and Capitalization

Cash and Equivalents:	**$86.6 million as of March 31, 2017**
Capitalization:	As of March 31, 2017
Common shares outstanding	42.2M
Options outstanding	4.9M
Total	**47.1M**
Cash Runway:	Anticipate current cash position could provide funding through Q1 2019
Other:	
Options available for grant	0.1M
Warrants (exercise price of $92.99 expiring September 2019)	0.2M

World-Class Clinical Advisory Board

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Lew Teperman, MD, Vice Chair of Surgery, North Shore University Hospital, Manhasset, NY

Russ Wiesner, MD, Professor of Medicine, Mayo Clinic

Win Williams, MD, Nephrologist, Massachusetts General Hospital (Harvard)

Investment Summary

- **Orphan cellular therapy designed to improve survival in acute forms of liver failure**
- **New phase 3 trial underway directed by data from prior VTI-208 trial**
  - **Topline results expected around mid-2018**
- **Unique market position and strong IP:**
  - **No other known bio-artificial liver in clinical trials in US or EU**
- **Multi-billion dollar market opportunity in each of US, EU and ROW**
  - **Orphan pricing and biologic margins lead to high value**
- **Plan to capture benefit in US and EU without partnership:**
  - **VTL owns all rights**