

CELLERANT  
THERAPEUTICS

***Myeloid Progenitors:  
An off-the-shelf cellular therapy***

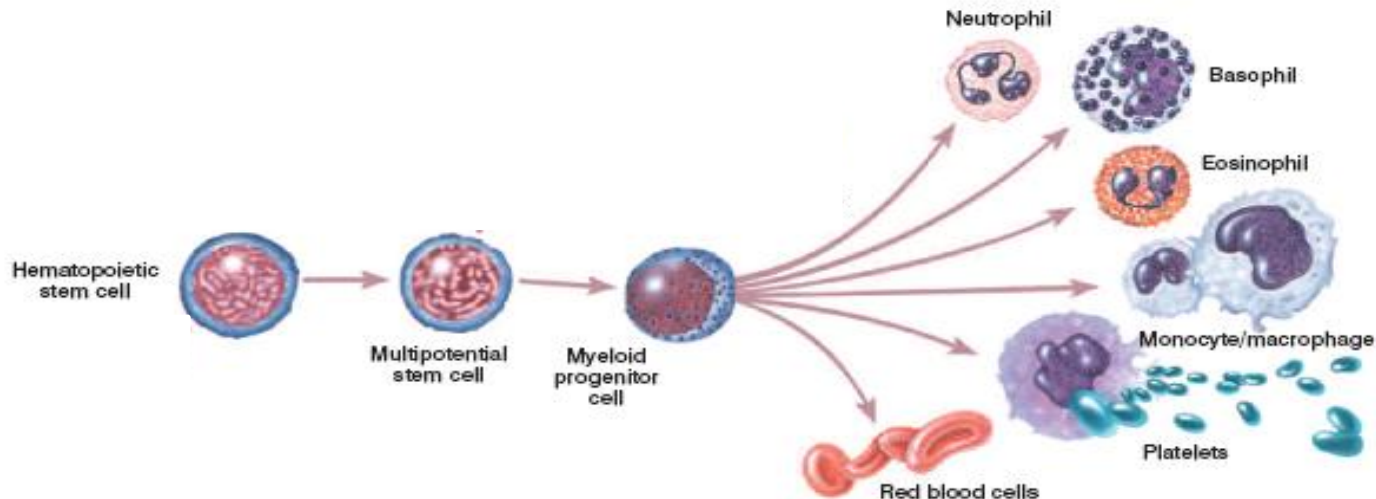
March 2013

## Company Overview

- **Founded in 2003**
  - Formed with exclusive technologies spun out of Novartis & Stanford
  - ~68 employees (~55 in R&D)
- **Developing therapies for unmet medical needs in the treatment of blood cancers and blood related disorders with orphan and accelerated approval paths**
- **CLT-008 lead program: Up to \$170 million in non-dilutive development contract funds CLT-008 through FDA Approval in three indications**
- **First-in-class, humanized antibody development candidate targeting unique antigen on AML cancer stem cells**

## Cellerant Expertise & Focus: Hematopoietic Biology

- Hematopoietic system is responsible for making all blood forming cells
- Severe Medical Conditions:
  - **Neutropenia** – reduction in neutrophils leading to infection & death
  - **Thrombocytopenia** – reduction in platelets leading to bleeding & death
  - **Leukemia** – proliferative disorders of the hematopoietic system



# Product Pipeline

Product	Discovery	Pre-Clinical	Phase 1	Phase 2	Phase 3
<b>CLT-008</b> Human Myeloid Progenitors (BARDA Funded)	Neutropenia in Acute Myeloid Leukemia (AML) patients		Ph 1/2		
	Cord Blood Transplantation in patients with Hem. Malignancies		Ph 1		
	Acute Radiation Syndrome		Animal Rule		
<b>CLT-009</b> Human Megakaryocyte Progenitors	Thrombocytopenia				
	Acute Radiation Syndrome				
<b>Cancer Stem Cell Antibody Program</b>	Acute Myeloid Leukemia (AML)				
	Myelodysplastic Syndrome (MDS)				
	Multiple Myeloma				

# LEAD PROGRAM

## CLT-008: Human Myeloid Progenitors

# The Problem: Unmet Needs – Chemo-induced Neutropenia / ARS



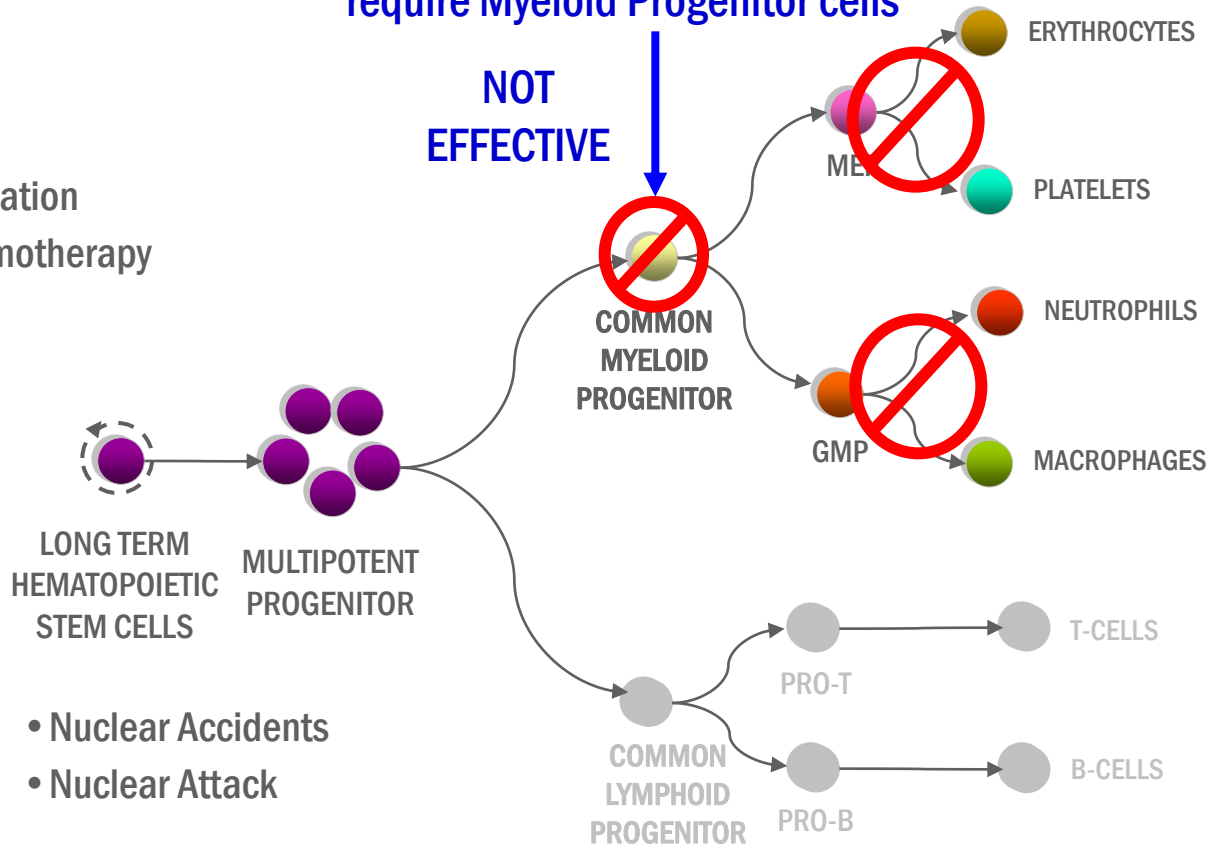
- Total Body Radiation
- High Dose Chemotherapy

**DESTROYS  
CIRCULATING  
CELLS**



- Nuclear Accidents
- Nuclear Attack

Current Treatments:  
G-CSF, GM-CSF: growth factors  
require Myeloid Progenitor cells



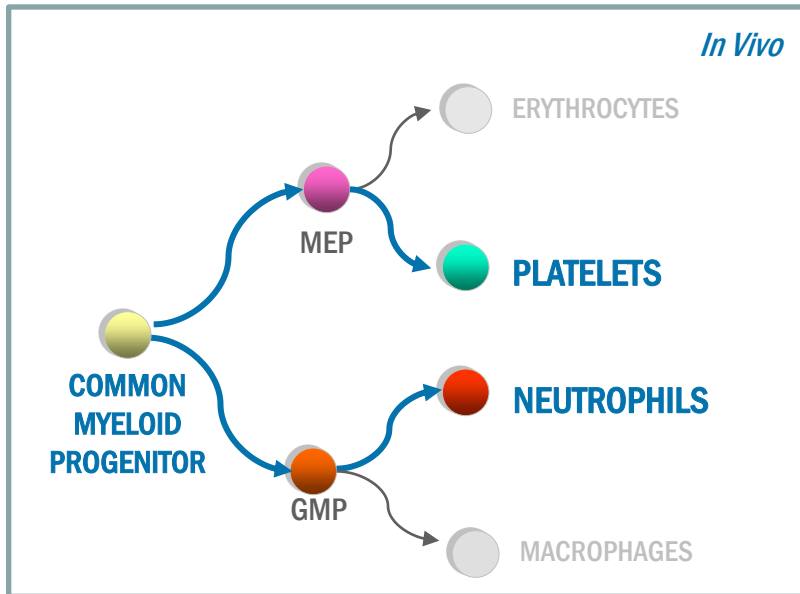
CLINICAL EFFECTS:

- Neutropenia
- Thrombocytopenia
- Infections
- Hospitalization
- Reduction in chemotherapy dose

# The Solution: CLT-008 Biological Rationale

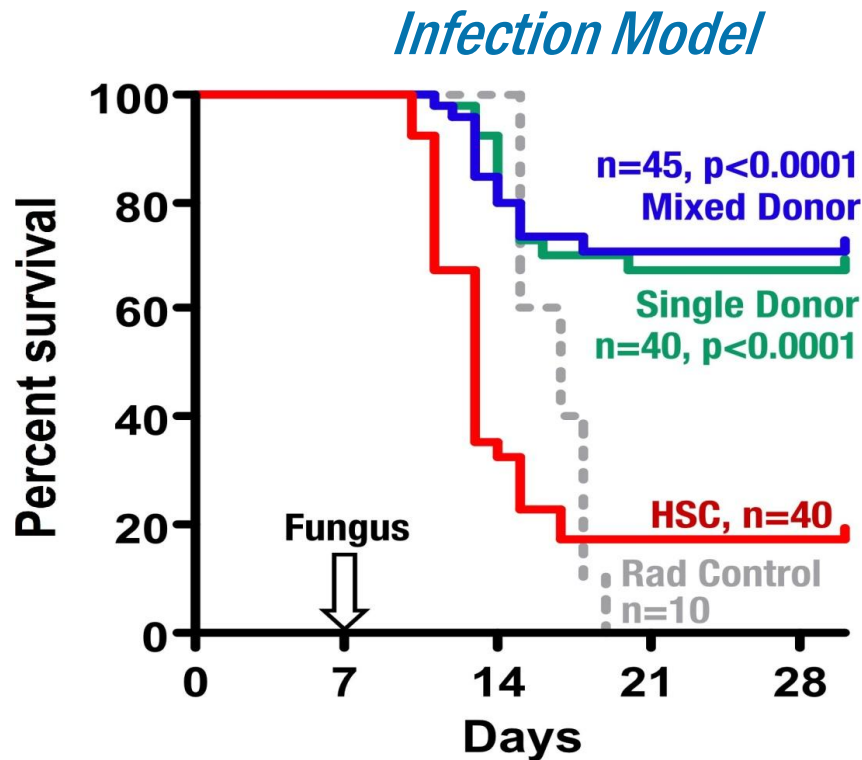


**CLT-008**



- **CLT-008 replenishes the body's myeloid progenitors**
- **Provides transient hematopoietic support**
- **Produces neutrophils and platelets in vivo**
- **Work synergistically with Standard of Care to increase production of neutrophils**

# CLT-008 Prevents Lethal Fungal Infection

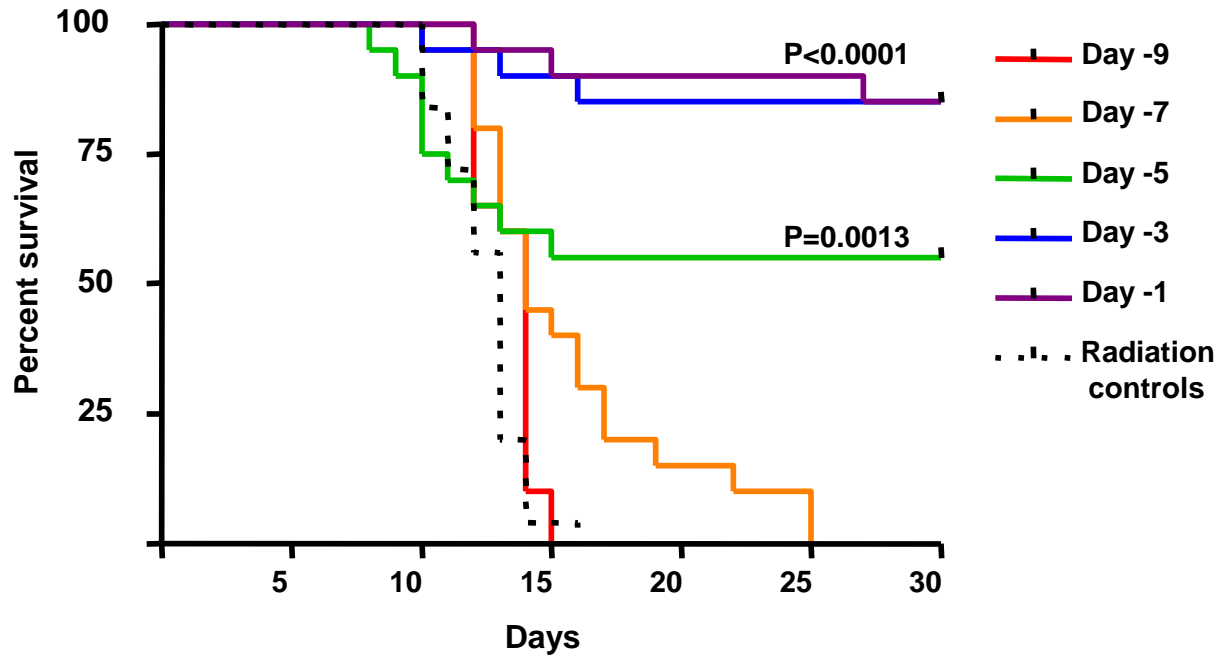


The figure combines survival data from 4 separate experiments. Lethally irradiated mice received 200 syngeneic HSC and 500,000 culture-derived allogeneic MPC (blue line) derived from a single donor (C57BL/Ka, H-2b) or 500,000 culture-derived MPC from at least three donors (C57BL/Ka, H-2b, FVB, H-2q, and AKR, H-2k) (green line). Survival is compared with mice receiving 200 syngeneic HSC without MPC (red line).



# CLT-008 Provides Protection from Lethal Radiation

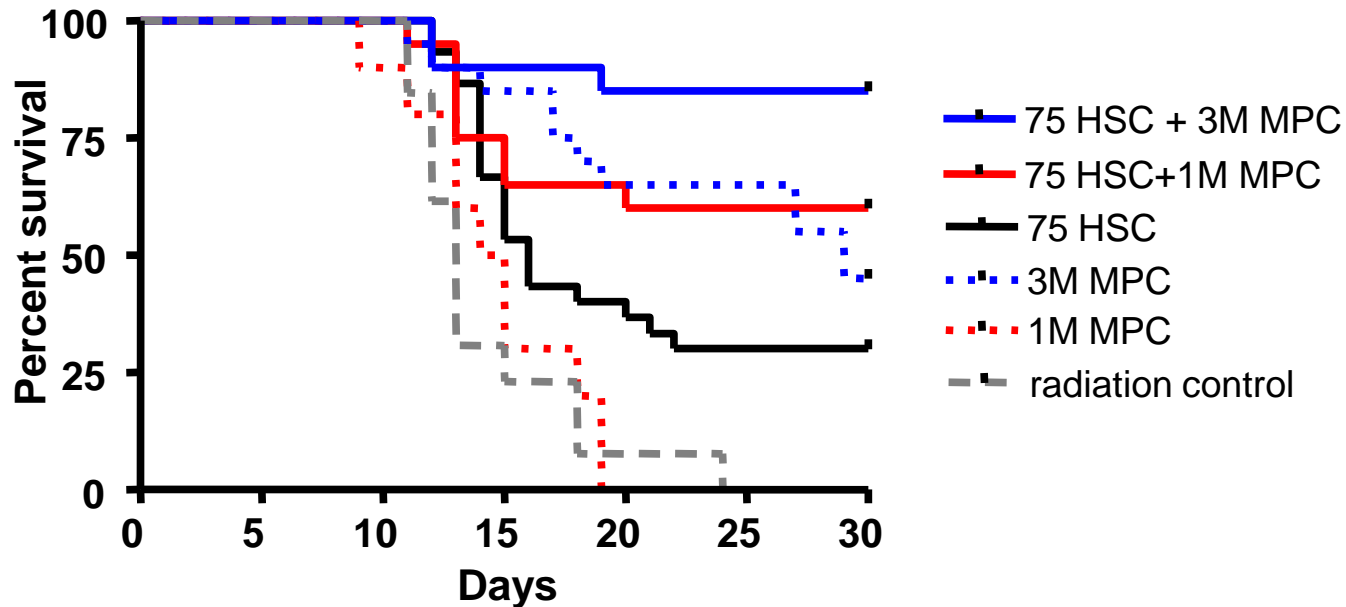
## *Nuclear Countermeasure Model*



- MPc provide radioprotection even if administered 5 days post irradiation (9Gy).
- The ability to delay administration of a radioprotectant is important in the setting of mass exposure when additional time may be required to triage and treat large numbers of people.

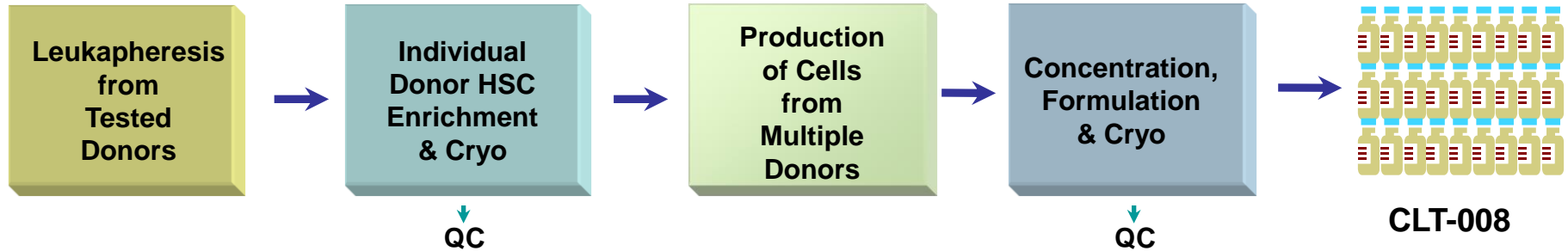
# CLT-008 Enables Engraftment with Sub-Optimal Stem Cell Dose

## *Stem Cell Transplant Model*



Balb/b mice (H-2b) were lethally irradiated and transplanted with 75 allogeneic C57Bl/Ka (H-2b) HSC or 75 HSC and 1 or 3 million MPC derived from AKR (H-2k) and FVB (H-2q). Additional cohorts of mice received only 1 or 3 million MPC. Co-infusion of HSC and 1 or 3 million MPC improved survival over mice receiving HSC only. Data combined from 3 experiments.

## CLT-008 Production Process



Universal off-the-shelf product available on demand

- Simple economical production process
- Reproducible in multiple donors
- Produced in large lots similar to other biologics
- Cryopreserved product, long shelf-life

## Product Characteristics

- Cryopreserved cells stored in vapor phase liquid nitrogen
- 5% DMSO final concentration
- No processing performed after thaw
- Infusion must be started within 60 minutes and completed within 120 minutes of 'thaw stop time'
- Required dosing volume is calculated for each patient based on specific product concentration to achieve desired cells/kg
- Product shipped with Certificate of Analysis and Certificate of Eligibility



# Example Certificate of Analysis for Final Product

- Lot specific Certificates will accompany each product shipment.

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**CERTIFICATE OF ANALYSIS**

**Product Code:** 00196241 **Lot Number:** CE0011-P  
**Product:** CLT-008 (CEL) **Manufacture Date:** 20-Aug-2010

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TEST (Method)	SPECIFICATIONS		Results
	Min.	Max.	
Cell Conc. by NucleoCounter (cells/ml)	31500000.0	38500000.0	33800000.0
Sterility-Direct Transfer	Negative	***	Negative
Endotoxin	< = 17.50	***	0.09 EU/ml
Mycoplasma, PTC	Negative	***	Negative
Viability by NucleoCounter	> = 70%	***	91 %
Phenotype (post-thaw)			
CD34+	> = 60%	***	98 %
CD15+	> = 5%	***	22 %
CD33+	> = 85%	***	100 %
CD19 + / CD33-	***	< = 0.50%	0.01 %
CD2 + / CD3 +	***	< = 0.10%	0.00 %
CD34 + / CD90	For Information Only	***	3.8 %

This lot of CLT-008 was manufactured from at least one donor who was reactive for antibodies to cytomegalovirus (CMV) using an FDA-cleared screening test, and should only be administered to recipients who are seropositive for CMV.

This lot has been reviewed by Quality Assurance in compliance with requirements of Lonza's Quality System.  
This document was generated from a validated Part 11-compliant electronic system and thus handwritten signatures are not required.

For Technical Assistance, call 1-800-521-0390

# CLT-008 – Starting Material

- Derived from G-CSF (Neupogen) mobilized peripheral CD34<sup>+</sup> blood cells of healthy, consenting donors
- Donors meet HCT/P eligibility criteria - test summary is listed on Certificate of Eligibility
- Lot-specific Certificates of Eligibility will be provided with CLT-008 product
- FDA has granted Cellerant an exemption from CFR1271.221(b), which prohibits pooling human cells or tissues from two or more donors during manufacturing

## CERTIFICATE OF SUBJECT ELIGIBILITY

Product Name: <b>Mobilized Peripheral Blood Mononuclear Cells</b>	
Subject number: 12168505	Product Number: W2597 10 801217 8 (1)
Collection Date: 11/1/2010	

### METHOD OF PREPARATION:

This peripheral blood mononuclear cell product was collected by apheresis on COBE Spectra from the subject following four daily injections of 780 µg of filgrastim (Neupogen®). All manipulations of the unit were performed without breaching the closed system in which it was collected and according to procedures compliant with current Good Manufacturing Practices (cGMP).

### ANALYSIS OF THE SUBJECT:

The subject completed the standard health history questionnaire used to evaluate donors of transfusable blood products and a supplemental questionnaire used to evaluate donors of Human Cells, Tissues, and Cellular and Tissue-based Products (HCT/Ps) as described in 21 CFR 1271 subpart C. The health history and supplemental questioning confirmed the subject met eligibility requirements for provision of these products for their intended use.

### ANALYSIS OF THE COMPONENT:

Blood samples collected from the subject within seven days preceding product collection were submitted for immunologic evaluation and infectious disease testing. Results are below:

Test	Result
ABO/Rh	O Rh Positive
Unexpected red blood cell antibody screen	Negative
Hepatitis B virus surface antigen	Negative (Non-reactive)
Antibody to hepatitis B virus core antigen	Negative (Non-reactive)
Hepatitis C virus antibody	Negative (Non-reactive)
Human T-cell lymphotropic virus types I and II antibody	Negative (Non-reactive)
Human immunodeficiency virus types 1 and 2 antibody	Negative (Non-reactive)
HIV-1 and HCV RNA by nucleic acid technology testing	Negative (Non-reactive)
West Nile Virus RNA by nucleic acid technology testing	Negative (Non-reactive)
<i>T. cruzi</i> antibody	Negative (Non-reactive)
Serological test for syphilis	Negative (Non-reactive)
Cytomegalovirus antibody	Positive

**Certified Communicable Disease Testing Laboratories Statement** [21 CFR 1271.55 (b)(1)]: Communicable disease testing was performed by testing laboratories certified to perform such testing on human specimens under the Clinical Laboratory Improvement Amendments and 42 CFR 493, or equivalent requirements as determined by the Centers for Medicare and Medicaid Services.

A. Scott Carter, Director of Medical Services and Customer Support  
 [Name, Title of Responsible Party] 11/1/2010  
 Date

**Statement of Donor Eligibility** [21 CFR 1271.55(a)(2)]:  
 Based upon a review of all screening and testing results this donor has been determined to be eligible.

A. Scott Carter, MT (ASCP) November 1, 2010  
 JANIE BALLARD FOR A. SCOTT CARTER *Janie Ballard for A. Scott Carter* November 1, 2010  
 Name of person completing COE Signature Date

# CLT-008 Lead Clinical Program

*Universal off-the-shelf product available on demand*

## CLT-008

- ❖ Human Myeloid Progenitors (hMPCs)
- ❖ Universal Cellular Therapy



## Product Profile

- ❖ Off-the-shelf, cryopreserved product
- ❖ No HLA matching required
- ❖ No GVHD expected
- ❖ Produce neutrophils & platelets in vivo

## Clinical Indications

- ❖ Neutropenia
- ❖ Cord Blood Transplantation
- ❖ Acute Radiation Syndrome

## CLT-008 Lead Clinical Program

### Target Indications:

- **Chemotherapy Induced Neutropenia**
  - Shorten the duration of neutropenia and thrombocytopenia
  - Reduce the risk of infections associated with high dose chemotherapy
  - Enable higher doses of chemotherapy
- **Hematopoietic Stem Cell Transplantation**
  - Facilitate engraftment following UCBT
  - Facilitate engraftment following suboptimal stem cell grafts
  - Decrease infections, mucositis and non-relapse mortality
- **Acute Radiation Syndrome**
  - Provide hematopoietic support until bone marrow recovers or as bridge to stem cell transplant



## CLT-008 Lead Clinical Program

- **Phase 1/2 Clinical Trial - Neutropenia**
  - Dose escalation trial of CLT-008 in patients receiving post-remission chemotherapy for acute leukemia (AML, ALL) or high risk myelodysplasia (MDS)
    - Dosed 20 patients to date
    - Doses well tolerated
    - No dose limiting toxicities observed
- **Phase 1 Clinical Trial – Cord Blood Transplantation**
  - Dose escalation/multiple dosing trial of CLT-008 in patients receiving chemotherapy and/or radiation followed by cord blood transplantation for the treatment of hematological malignancies
    - Dosed 20 patients to date
    - Doses well tolerated
    - No product related dose limiting toxicities observed

## CLT-008 Lead Clinical Program

- Current Phase 1/2 clinical trials are in the target patient population
- Working closely with BARDA and FDA in clinical development strategy
- Registration Strategy
  - Accelerated Path/Orphan Designation
    - Approval in AML patients
    - Approval in patients with hematological malignancies undergoing cord blood transplantation
  - Label expansion into other cancer patients (e.g. solid tumors)

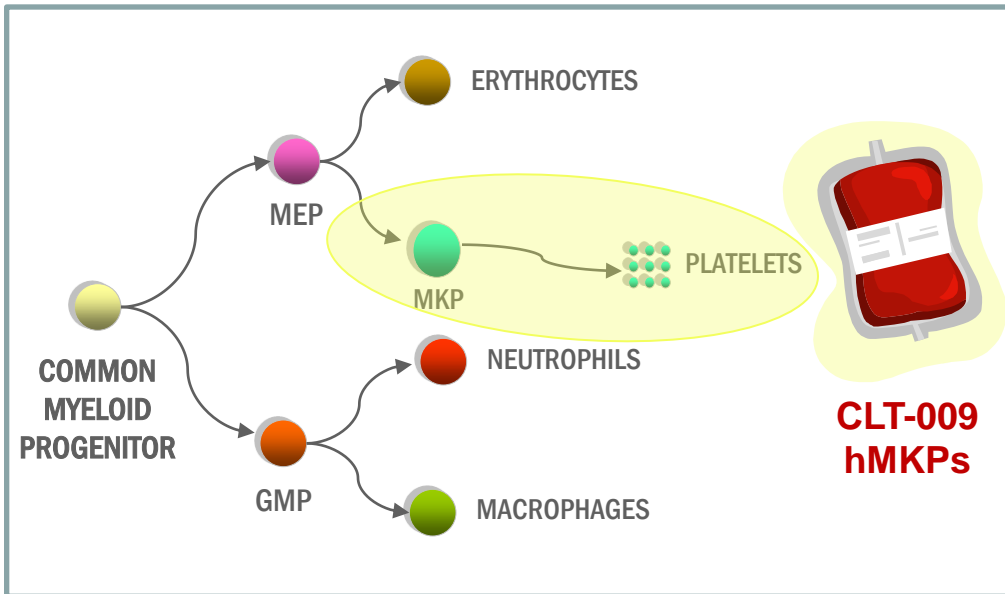
# PRODUCT PIPELINE:

## CLT-009: Human Megakaryocyte Progenitors

# CLT-009 Program

## CLT-009

- ❖ Human Megakaryocyte Progenitors (hMKPs)
- ❖ Universal Cellular Therapy



## Product Profile

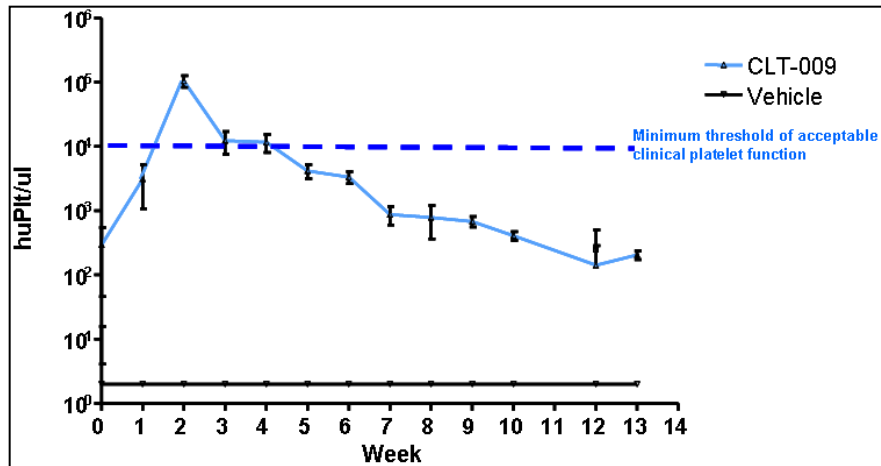
- ❖ Off-the-shelf, cryopreserved product
- ❖ No HLA matching required
- ❖ No GVHD expected
- ❖ Produce platelets in vivo

## Clinical Indications

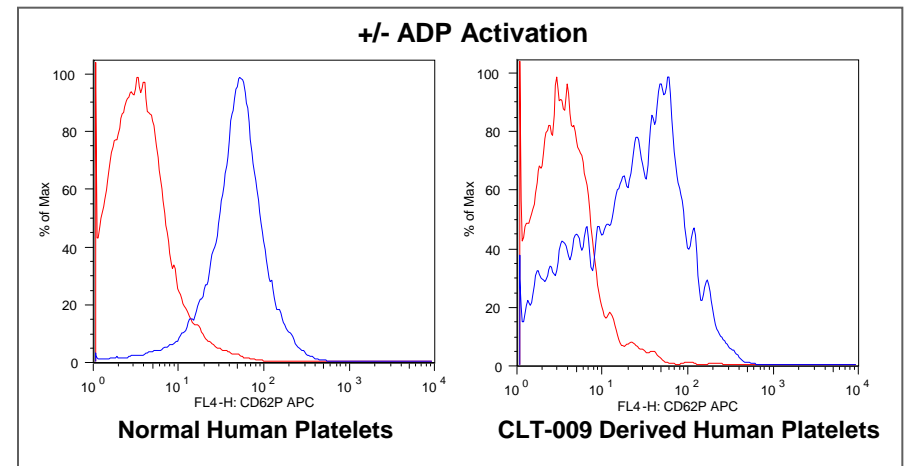
- ❖ Thrombocytopenia
- ❖ Acute Radiation Syndrome

# CLT-009 Produces Functional Platelets *In Vivo*

CLT-009 makes platelets



CLT-009 makes functional platelets



- Demonstrates ADP-dependent platelet activation competency of platelets generated *in vivo*
- Similar to activation observed for normal human platelets collected from patients

## Summary

*Developing first-in-class products for unmet medical needs in the treatment of blood cancers and blood related disorders with orphan and accelerated approval paths*

# Management Team

Name	Position	Experience
Ram Mandalam, PhD	President & CEO	Geron, Aastrom Biosciences
Margaret Dillon, PhD	Sr. VP, Regulatory Affairs & Quality Assurance	CV Therapeutics (Gilead), Systemix (Novartis), Schering-Plough
Sean Givens	VP, Government Operations & Controller	Microfluidic Systems, Bechtel, Varian, Optiovison, ONI Systems
William Reed, MD	VP, Clinical Development	Cerus Corp, Blood Systems Research Institute, UCSF
Robert Tressler, PhD	VP, Research & Development	Geron, Genencor, Matrix, Chiron, Syntex (Roche)
Jun Yoon	VP, Corporate Development	VIA Pharma, Sagres Discovery (Chiron), Syrrx (Takeda)

## Board of Directors

Name	Position
Lowell Sears (Chairman of the Board)	Chairman & CEO, Sears Capital Management, Former CFO, Amgen
Richard Chyette	General Counsel, QuickenLoans
Steve Greenberg	Managing Director, Allen & Company
Ram Mandalam	President & CEO, Cellerant Therapeutics
Richard Rathmann	Managing Director, GBR Investments
Gisela Schwab	EVP and Chief Medical Officer, Exelixis