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

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

CLT-008: Human Myeloid Progenitors
The Problem: Unmet Needs – Chemo-induced Neutropenia / ARS

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

NOT EFFECTIVE

DESTROYS CIRCULATING CELLS

• Total Body Radiation
• High Dose Chemotherapy

• Nuclear Accidents
• Nuclear Attack

CLINICAL EFFECTS:
- Neutropenia
- Thrombocytopenia
- Infections
- Hospitalization
- Reduction in chemotherapy dose

• Nuclear Accidents
• Nuclear Attack

CURRENT TREATMENTS:
- G-CSF, GM-CSF: growth factors require Myeloid Progenitor cells

NOT EFFECTIVE
The Solution: CLT-008 Biological Rationale

- 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

Infection Model

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).
• 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

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

- 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.
CLT-008 – Starting Material

- Derived from G-CSF (Neupogen) mobilized peripheral CD34+ 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
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*

- 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

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

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