Controlling cell death to protect human life

NewsMakers in the Biotech Industry
October 22, 2010
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CBLI is developing drugs against:

- Radiation damage, side effects of chemotherapy and acute stresses
- Cancer
# CBLI Summary

- **Incorporated in June 2003**
  - Spin-off from the Cleveland Clinic
- **NASDAQ listed since 2006**
  - Ticker: CBLI
- **HQ - Buffalo, NY**
  - 44 full time employees (majority PhDs & MDs)

## Funding History

- Money raised from capital markets: $56 million
- Federal grants and contracts: $65 million
- DoD option to purchase CBLB502: $30 million

## Partnerships

- Cleveland Clinic (CCF)
- Roswell Park Cancer Institute (RPCI)

## IP

- Multiple sets of patent applications filed
- **First CBLB502 and CBLB612 patents granted**
CBLI Market Opportunities (major drug candidates)

Protection from Acute Radiation Syndrome (ARS)
~$500 million (no competing approved products)
**CBLB502**

Reduction of cancer treatment side effects
~$20 billion (70% of patients experience dose and regimen limiting toxicity and need supportive care)
**CBLB502, CBLB612**

Direct-acting anti-cancer drugs
~$50 billion (limited improvement in cancer survival over the last 30 years)
**CBLC102, CBLC137**
Underlying Science and Origin of CBLI Drugs

- Understanding of the role of apoptosis (regulated cell death) in multiple human diseases
- Bacterial signaling factors as drug candidates to temporarily suppress apoptosis
- New class of DNA-intercalators with direct anti-cancer activity
- Hematopoietic stem cell induction for supportive care in cancer treatment

Basic research lead by CBLI’s Dr. Andrei Gudkov at the Cleveland Clinic and Roswell Park Cancer Institute
CBLB502
Defense Application
Acute Radiation Syndrome (ARS)
ARS Caused by Nuclear Attack
Customer Viewpoint

• A nuclear attack has been identified by President Obama and global leaders as a **number one security threat**

• A terrorist attack with a **10 KT device will kill 400,000 people** in NYC most of them via ARS (Institute of Medicine Report, June 2009)

There is no approved drug which can effectively protect from ARS
CBLB502 for ARS (Summary)

- **DoD Contract**: $45 million including development funding and conditional purchase commitment, awarded September 2010
- **Efficacy**: experiments with hundreds of primates show unprecedented efficacy of the drug with single administration
- **FDA Process**: Open IND in 2007, multiple meetings and ongoing dialogue, fast track granted July 2010
- **Completed human trials**: 50-subject dose-escalation human safety trial concluded June 2009, 100-subject second human safety trial concluded September 2010
- **Government development support**: $47 million in development contracts from DoD, BARDA/HHS and NIAID/NIH received 2008-2010 (~$20 million left), pending proposals for additional $50 million
CBLB502: Mechanism of Action

Multiple mechanisms of radiation defense

Protection from two major components of radiation death: gastrointestinal (GI) and hematopoietic (HP) syndromes
CBLB502 Efficacy: Survival (Mitigation) after LD70 IR

Effective when injected up to 48 hours after radiation
CBLB502: Organ and tissue recovery of lethally irradiated primates

Pathology data demonstrates protection of GI tract, blood, immune system and skin
50% subjects have no observed abnormalities on day 40
Animal Efficacy Rule – Path to FDA licensure

- Compliance with CMC requirements
- Efficacy in two animal species including rhesus macaques (survival as endpoint)
- Safety in healthy humans
- Well understood mechanism of action (to provide biomarkers of efficacy)

Established FDA pathway to approve drugs where efficacy is unethical to test in humans
cGMP Production of CBLB502: CMC Participants

- Laboratory Strain
- Production Strain, DSP
- Cell Bank
- QC protocols, stability
- Bioassay
- Test Residuals
- Preclinical Trials
- Formulation
- Fermentation Improvement
- Status: High-yield cGMP process
- Final formulation
- Stability studies ongoing

Cleveland BioLabs, Inc
### CBLB502 ARS: Summary of Primate Studies

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<th>Parameter</th>
<th>Time relative to TBI (if applicable)</th>
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<td>Thrombocytopenia reduction</td>
<td>+++</td>
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**Data on dose dependence of efficacy** √

+++: strong effect; ++: moderate effect; +: minor effect; √: data collected

**Status:** >20 studies with over 800 primates tested dose-dependence for the drug, efficacy time window and effects of various radiation doses.
Summary of Human Trials of CBLB502

• Dose limiting toxicity (DLT) defined
• Most common adverse effect was “flu-like syndrome”
• Majority of adverse effects were mild or moderate
• Majority of effects are extremely transient (<2-4 hours)
• Adverse event profile described; predictable and related to the known pharmacology of CBLB502
• **Calculated efficacious dose in humans is below DLT (calculations based on protective dose in primates and biomarker analysis)**
• **All biomarkers project similar efficacious human dose**
CBLB502: Development Tasks Left

- CMC: consistency runs
- Efficacy: Pivotal animal study
- Human safety: Phase IIB trial
- Submission of BLA
Primary sales targets: Need understood, concepts of use developed, high degree of financial commitment, relations with CBLI in place
- DoD, BARDA/HHS, Israel
- “Buying” RFPs for US agencies out or expected next year
- Hundreds of millions of dollars allocated for initial purchase among US agencies

Secondary sales targets: Serious public concern, policies being developed
- UK, Canada, India, China, Japan, S. Korea
- Some initial contacts with CBLI

Projected addressable market ~$500 M/year (w/penetration over time)
No competing products today
Contract from DoD indicates commitment to procurement
CBLB502
Medical Applications
CBLB502 as Radiation Therapy Adjuvant (total body irradiation)

- Rescues animals from radiation toxicity
- Potentiates effect of radiotherapy
- Allows radiation dose escalation
- Does NOT protect tumor
CBLB502: Protection from Focused Split-Dose Irradiation

Strong mitigation of radiological damage of healthy tissues shown in mouse model of head-and-neck damage directly supports first medical trial

X-ray

3x10 Gy daily

3x10 Gy daily with CBLB502 pretreatment

Body weight, %

Days

10 Gy x3  (CBLB502 + 10 Gy) x3

60 70 80 90 100 110

0 5 10 15
CBLB502 Clinical Program
Phase I/II Head & Neck Human Trial

• Open IND

• Funded by $5.3 million stimulus grant received September 2009

• Protocol discussed with Scientific Review Committee

• Planned to start at Roswell Park Cancer Institute and other centers 2010
Qualitative effect on survival from lethal dose of chemotherapy (Cisplatin) in mouse model
CBLB612
Stem Cell Inducing Agent
Dramatic improvement of blood recovery during Cyclophosphamide treatment in mice
CBLB612 is 6x more efficacious than G-CSF and induces both early and late progenitor cells. Effects of CBLB612 and G-CSF are synergistic.
CBLB612: Product Development Strategy

6-month Phase I safety study in healthy volunteers enables full assessment of induction and mobilization of stem cells in peripheral blood, a direct predictor of efficacy of the drug

**Zhejiang Hisun Pharmaceutical license for China**
**signed Sept. 2009**
**($1.65M upfront development, 10% royalties)**

**Principle efficacy assessment in Phase I = potential partnering**
Curaxins
Anti-cancer drugs
Curaxins: Overview

• First-in-class broad-spectrum anticancer drugs
• Small molecules suitable for oral administration
• Novel mechanism of action – simultaneous targeting three major pathways deregulated in cancer
• Composition of matter patent applications
• Efficacy in multiple animal models of major cancer types including breast and prostate cancer
• Proof of concept Phase II trial in prostate cancer
Incuron – JV for Curaxin Development

• 50/50 joint venture with Bioprocess Ventures, Moscow

• ~$18M to reach Phase II for new generation of Curaxins in US and conduct human trials in liver cancer in Russia for CBLC102

• CBLI oversees mechanistic studies and formal development
Extended Pipeline (backburner compounds)

- Anti-apoptotic compounds against reperfusion injury (acute renal failure, tourniquet, etc.)
- Anti-myc and anti-androgen-receptor compounds in cancer treatment
- MRP inhibitors in cancer treatment
- Others
Financial Summary

- Market cap (over last 3 months): $90-140M
- Shares Outstanding: 27M common, 40M fully diluted
- Government Grants & Contracts support CBLB502 for defense and limited medical applications: $20M unspent (excl. $30M option for first purchase), $50M pending
- CBLI subsidiary Incuron funds Curaxin development for next three years: $18M
- CBLI Cash & Receivables (at 6/30/10): $7.2M (CBLI only), $3.2M (Incuron)
- Avg. Monthly Burn Rate (on CBLI cash): $200,000 (CBLI only)
Senior Management Team

Chief Executive Officer & President
Michael Fonstein, PhD
- Scientist and serial entrepreneur
- Founder of Dia-M and The Fellowship for Interpretation of Genomes (FIG)
- Founder and Former CEO of Integrated Genomics, Inc. (’97-03)

Chief Financial Officer
Jack Marhofer, MBA, CMA, CFM
- 20 years of financial and accounting experience
- 8 years as a corporate controller of a public company

Chief Operating Officer
Yakov Kogan, PhD, MBA
- Former Director of Business Development at Integrated Genomics, Inc.
- Expert in technical sales and contract negotiations

Chief Scientific Officer
Andrei Gudkov, PhD, D.Sci
- SVP of Basic Science, Roswell Park Cancer Institute
- Former Chair, Dept. Molecular Biology at Cleveland Clinic
- 30+ issued patents
- 150+ research publications

Chief Medical Officer
Michael Kurman, MD
- 25 years global oncology drug development experience
- Senior positions in clinical operations at CROs
- Led clinical development in several publicly traded biotech companies

Executive Vice President, Regulatory Affairs and Quality Assurance
Ann Hards, PhD
- Over 20 years of regulatory experience at large and small pharma
- Multiple successful NDAs, MAAs, sNDAs, advisory committees
## Boards

### Board of Directors

**Independent Directors**

- Bernard L. Kasten, MD  
  Former CEO, SIGA Technologies

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  Former CEO & President of Berlex Biosciences, a Division of Bayer AG

- James Antal, CPA, MBA  
  Former CFO and CIO of Experian

- Paul DiCorleto, PhD  
  Chairman, Lerner Research Institute

**Management**

- Michael Fonstein, PhD  
  CEO & President, Cleveland BioLabs, Inc.

- Andrei Gudkov, PhD, DSci  
  CSO, Cleveland BioLabs, Inc

- Yakov Kogan, PhD, MBA  
  COO, Cleveland BioLabs, Inc

### Scientific Advisory Board

- **George R. Stark, PhD**  
  Chairman of SAB, Member of NAS, Former director of LRI, Scientific Advisor to Amersham and Genentech, pioneered numerous major research technologies

- **Inder Verma, PhD**  
  Member of NAS, Professor of Salk Institute, Founder and Scientific Advisor to Cell Genesys, Signal Pharmaceuticals, UroGenesys, Ventana Pharmaceuticals, Quark Biotech. Internationally recognized leader in cancer biology and inflammation

- **Bruce Blazar, MD**  
  Professor, Chair in Transplantation Immunology of University of Minnesota. Member of the FDA Advisory Committee, SAB member of BioMarin Pharmaceutical, Seattle Genetics, etc.