Bellicum PHARMACEUTICALS

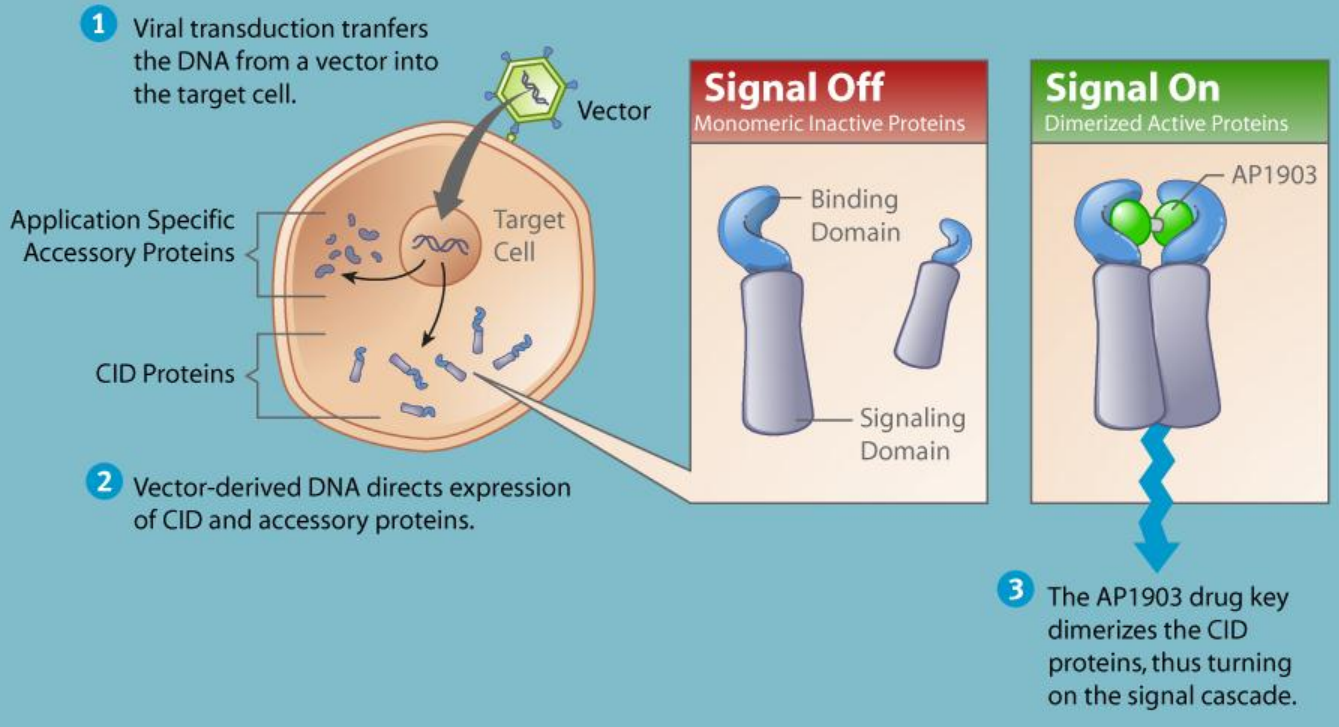
CPRIT Annual Conference Company Showcase

CaspaCIDe™ (BPX-501) Project Update

October 25th, 2012

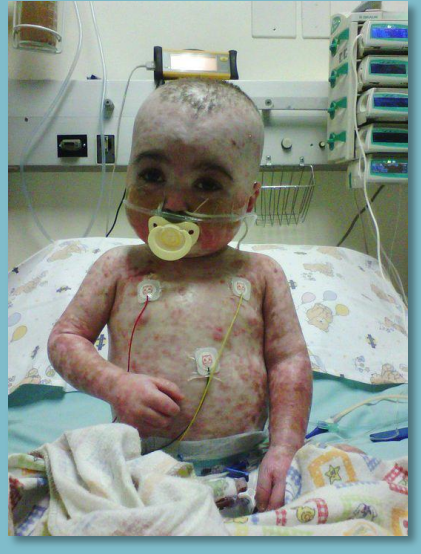
Tom Farrell, President & CEO

Chemical Induction of Dimerization (CID)



Unmet Medical Need: GvHD

- **Allogeneic hematopoietic stem cell transplantation (HSCT)**
  - Replace patient's immune system with healthy donor stem and T cells
  - Often curative for patients with leukemia, lymphoma and other cancers
  - 30-60% mortality @ 1 year



- **Graft vs. Host Disease**
  - T cells from the donor ("Graft") attack the patient's healthy tissue ("Host")
  - Attacks the skin, mucosa, intestines and liver, with debilitating consequences
  - Occurs in 30-80% of HSCT patients, and is often fatal
  - Incidence and severity greatest where donor and patient are mismatched (e.g. parent-child)
- **Solution: CID switch to eliminate GvHD-causing T Cells**

Clinical Proof of Principle – NEJM Article & Editorial

The NEW ENGLAND JOURNAL of MEDICINE

ORIGINAL ARTICLE

Inducible Apoptosis as a Safety Switch for Adoptive Cell Therapy

Antonio Di Stasi, M.D., Siok-Keen Tey, M.D., Gianpietro Dotti, M.D., Yuriko Fujita, M.D., Alana Kennedy-Nasser, M.D., Caridad Martinez, M.D., Karin Straathof, M.D., Enli Liu, M.D., April G. Durett, M.Sc., Bambi Grilley, R.Ph., Hao Liu, Ph.D., Conrad R. Cruz, M.D., Barbara Savoldo, M.D., Adrian P. Gee, Ph.D., John Schindler, Ph.D., Robert A. Krance, M.D., Helen E. Heslop, M.D., David M. Spencer, Ph.D., Cliona M. Rooney, Ph.D., and Malcolm K. Brenner, M.D.

ABSTRACT

BACKGROUND

Cellular therapies could play a role in cancer treatment and regenerative medicine if it were possible to quickly eliminate the infused cells in case of adverse events. We devised an inducible T-cell safety switch that is based on the fusion of human caspase 9 to a modified human FK-binding protein, allowing conditional dimerization. When exposed to a synthetic dimerizing drug, the inducible caspase 9 (iCasp9) becomes activated and leads to the rapid death of cells expressing this construct.

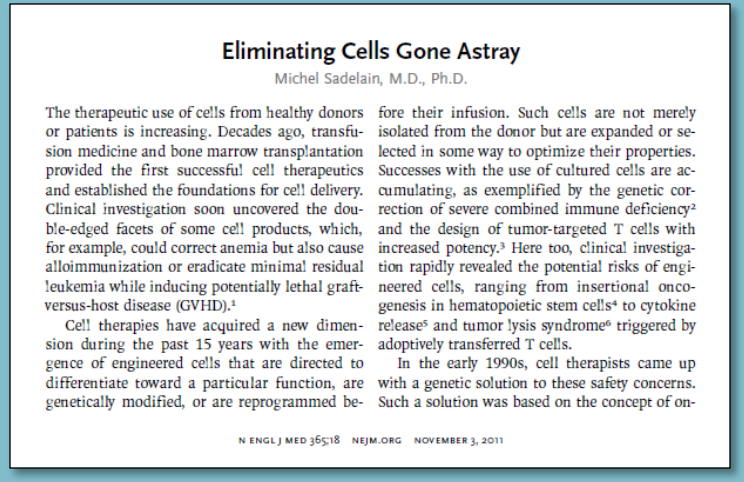
METHODS

We tested the activity of our safety switch by introducing the gene into donor T cells given to enhance immune reconstitution in recipients of haploidentical stem-cell transplants. Patients received AP1903, an otherwise bioinert small-molecule dimerizing drug, if graft-versus-host disease (GVHD) developed. We measured the effects of AP1903 on GVHD and on the function and persistence of the cells containing the iCasp9 safety switch.

From the Center for Cell and Gene Therapy, Baylor College of Medicine, Texas Children's Hospital and Methodist Hospital, Houston (A.D.S., S.-K.T., G.D., Y.F., A.K.-N., C.M., K.S., E.L., A.G.D., B.G., H.L., C.R.C., B.S., A.P.G., R.A.K., H.E.H., D.M.S., C.M.R., M.K.B.); and the University of Texas Southwestern Medical School, Dallas (J.S.). Address reprint requests to Dr. Brenner at the Center for Cell and Gene Therapy, Baylor College of Medicine, 1102 Bates Ave., Suite FC 1660, Houston, TX 77030, or at mbrenner@bcm.edu.

Drs. Di Stasi and Tey contributed equally to this article.

N Engl J Med 2011;365:1673-83.



Eliminating Cells Gone Astray

Michel Sadelain, M.D., Ph.D.

The therapeutic use of cells from healthy donors or patients is increasing. Decades ago, transfusion medicine and bone marrow transplantation provided the first successful cell therapeutics and established the foundations for cell delivery. Clinical investigation soon uncovered the double-edged facets of some cell products, which, for example, could correct anemia but also cause alloimmunization or eradicate minimal residual leukemia while inducing potentially lethal graft-versus-host disease (GVHD).[1]

Cell therapies have acquired a new dimension during the past 15 years with the emergence of engineered cells that are directed to differentiate toward a particular function, are genetically modified, or are reprogrammed before their infusion. Such cells are not merely isolated from the donor but are expanded or selected in some way to optimize their properties. Successes with the use of cultured cells are accumulating, as exemplified by the genetic correction of severe combined immune deficiency[2] and the design of tumor-targeted T cells with increased potency.[3] Here too, clinical investigation rapidly revealed the potential risks of engineered cells, ranging from insertional oncogenesis in hematopoietic stem cells[4] to cytokine release[5] and tumor lysis syndrome[6] triggered by adoptively transferred T cells.

In the early 1990s, cell therapists came up with a genetic solution to these safety concerns. Such a solution was based on the concept of on-

- **Recognized by the Clinical Research Forum as one of the "Top 10 Clinical Research Achievements" of the past 2 years**

Bellicum PHARMACEUTICALS

CPRIT-Funded Product Candidate: BPX-501

- **BPX-501: T cells from donor genetically modified with CaspaCIDe vector**
- **Indication: Treatment of high risk hematologic malignancies**
- **AP1903 used to treat GvHD, if it develops**
- **Addresses major unmet medical need in treatment of GvHD:**

Market Need	Standard of Care	BPX-501 + AP1903
Rapid resolution	✗ (weeks/months)	✓ (1-2 days)
Broad efficacy	✗ (35% 14 day cure rate)	✓ (100% 2 day cure rate)
Non-immunosuppressive	✗	✓

- **Primary clinical application is graft engineering of a mismatched transplant**
  - Twice as many patients can receive a potentially curative transplant

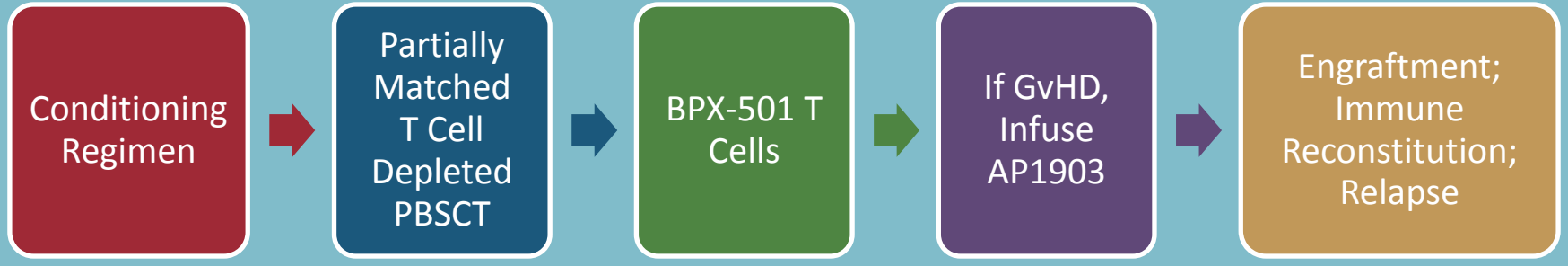
Bellicum PHARMACEUTICALS

Key Accomplishments Award Year One

- **Staff expanded from one to 14**
  - Clinical, manufacturing, regulatory, QA and scientific leadership in place
  - In-house research and process development lab established
- **Clinical grade raw materials manufactured and released**
- **Process for manufacture of BPX-501 T cell product substantially improved**
  - Original open process now functionally closed
- **cGMP facility with capacity for 20 patients per month constructed**
- **Extensive formal preclinical pharmacology/toxicology studies completed**
- **Clinical protocol finalized, with input from transplant centers nationwide**
- **IND allowed by FDA on October 19th**

BPX-501 Protocol Overview

- **Mismatched transplants in adults & children with hematologic malignancies**
  - Primary trial sites include Baylor Dallas, UT Southwestern, Fred Hutchinson, Memorial Sloan Kettering, Ohio State, Oregon Health Science, University Hospitals of Cleveland



- **Outcomes: engraftment, immune function & relapse (3, 6 & 12 month endpoints)**
- **Second protocol in matched, reduced conditioning patients at MDACC**

$37.5 MM Cumulative Non-Traditional Financing

- **$10 million cumulative equity capital raised through late 2010**
  - local high net worth individuals
- **$1.45 million ETF award supported BPX-101 pre-IND and Phase 1/2**
- **$6 million CPRIT award supports BPX-501 development**
- **$20 million Series B financing closed March 2012**
  - Non-traditional venture funds
    - AVG Ventures
    - Remeditex Ventures
  - >50% insider participation

Certified 100% Texas Raised!