One Mission: Eradicate AIDS

November 2013
Company Overview

- Clinical stage, leading developer of curative AIDS therapies

- Gene-based cell therapeutic technology developed by Dr. David Baltimore (Nobel Laureate) driven by revolutionary discoveries in AIDS biology and robust scientific evidence

- First therapeutic candidate (Cal-1) is in US Phase I/II trial
HIV/AIDS – A Global Epidemic with Enormous Costs

- 34.1M people living with HIV/AIDS
- >2.2M a year newly infected
- Only ~10% well-controlled on therapy
- Drug maintenance very expensive
  - Annual drug therapy cost >$25k
  - Lifetime cost exceeds $750k
- Still no cure

HIV/AIDS Treatment Costs
- $20B

Additional Care Costs
- $20B

Worldwide Annual Total
- $40B
HIV/AIDS – Limitations in Care

- Standard of care is daily regimen of highly-active antiretroviral therapy (HAART)
- HAART typically includes 3 antiretroviral drugs from 2 different classes
- 5 drug classes exist

Complications with HAART

- Co-morbidities after 15-20 years
- Low patient adherence (<60% in US)
- No long-term immunity; not a cure
- Requires a lifetime of therapy
- Very costly
HIV/AIDS: Path to a Cure
Berlin Patient – The First Functional HIV Cure

Proof of Concept Achieved in Man

- In 1996, CCR5 discovered to be co-receptor used by HIV to infect cells
  - Most people inherit two normal copies of gene that codes for CCR5 protein
  - ~1% of European population lacks both copies of the gene and resist HIV infection
- In 2007, Dr. Gero Hutter treated HIV/Leukemia patient in Berlin with CCR5-neg donor cells
- Patient has no detectable HIV or leukemia 6 years after treatment
- American Foundation for AIDS Research has declared patient “functionally cured”
Important Lessons from the Berlin Patient

- CCR5 expression is required for maintenance of HIV infection
- Conversion to cells with natural mutation (lacking CCR5 expression) drives HIV viral load to undetectable
- Transplanted stem cells can produce T cells that are resistant to HIV and can re-populate the individual
Calimmune: Engineering Immunity
Calimmune’s Strategy to Engineer Immunity

- Protect T-Cells by downregulating the CCR5 receptor to block attachment
- Prevent fusion using a next generation fusion inhibitor
  - Fusion inhibitors introduced as a new class of antiretroviral drugs in 2003
  - Effective against all tested HIV strains
- Modify CD4+ T Cells for short to medium-term protection AND CD34+ stem cells to sustain “new” immune system that renders the virus clinically irrelevant
Cal-1 – Potent Modification of a Patient’s Cells

- Combination therapy (sh5 and C46) to prevent attachment, fusion, and entry

**Sh5 to Down-regulate CCR5**
- Selected from library of >1600 clones
- Active against all tropic forms of HIV-1 (*in vitro* and *in vivo*)
- 10 yrs of simian safety data

**C46 to Inhibit Fusion**
- Over a decade of development (J&J and Dr. Von Laer)
- Engineered for expression on cell membrane; no systemic toxicity
- Strong anti-HIV activity
- Successful Ph I w/ no immunogenicity

- Internal promoters introduced via self-inactivating lentiviral vector drive sh5 and C46 with consistent expression
A One-Time, Outpatient Procedure

- Ex-vivo gene therapy to modify CD4+ T Cells and CD34+ Stem Cells
- Reintroduction of cells to create a new immune system
US Phase I/II Study

Design and Primary Objectives
- Ex-vivo gene therapy to modify CD4+ T Cells and CD34+ Stem Cells
- Reintroduction of cells to patients with varying levels of busulfan
- 12 total patients

Dosing Arms
- 12 total patients; 3 cohorts:
  - Transduced (4)
  - Transduced + low dose busulfan (4)
  - Transduced + intermediate dose busulfan (4)

Primary Endpoints
- Safety
- Feasibility

Secondary Endpoints
- Marking/expression
- Viral load
- T-cell count
- Thymopoiesis
- Progression of HIV disease
US Clinical Progress

- Enrolment of first cohort is almost complete
- Second cohort will start after data review by DSMB