Cancer vaccines offer therapeutic and preventative benefits with no associated toxicity. Unlike chemotherapeutic agents, vaccines also target and destroy cancer stem cells, potentially halting the progression and reoccurrence of disease. Vaccines based on our two proprietary antigens, MUC1 and Cyclin B1, may be an effective method of attacking and preventing a number of different adenocarcinomas, including pancreatic, breast, colorectal, ovarian, kidney, lung and prostate cancers.

Cancer vaccines represent enormous commercial potential driven by:
- 8.4 M cancer patients, $110B annual healthcare costs (U.S)
- BRCA2.
- Lack of effective treatment options for a frequently fatal disease.
- Increased public awareness.

The ability to take a vaccine beyond animal testing and collect Phase I clinical data is critical to attracting capital, even if such data comes from only one institution. Once such clinical data is available, however, corporate and institutional investors have shown great recent interest.

### Invention 1: MUC1 Vaccines for Therapy and Prevention of Cancer

- Abnormal MUC1 overexpressed on all human adenocarcinomas (~85% of human tumors), premalignant lesions and cancer stem cells.
- Immune response against abnormal MUC1 elicited through vaccination controls tumor growth without autoimmunity.
- Vaccines with synthetic abnormal MUC1 peptides and glycopeptides can elicit or boost immunity in some cancer patients resulting in increased disease-free survival and better outcome.
- Vaccines given to high-risk individuals to prevent tumor development would not be compromised by tumor-induced immunosuppression, suggesting a better outcome.

Current prophylactic application: A clinical trial reviewed and endorsed by the FDA (IND pending), proposes to vaccinate patients with advanced adenomas at high risk for recurrence.

### MUC1 Vaccine Clinical Trials at the University of Pittsburgh

- 1993-1995: Phase I in advanced pancreatic, breast and colon cancer patients who failed standard therapies (63 patients)
- 100mer MUC1 peptide plus BCG
- 1996-2001: Phase II in breast cancer patients undergoing autologous stem cell transplantation
- 100mer MUC1 peptide plus GM-CSF
- 2000-2003: Phase II/III in resected pancreatic cancer, prior to standard therapy (18 patients)
- 2003-2004: Phase II/III in resected pancreatic cancer prior to standard therapy (18 patients)
- 2006-2007: Phase III/IV in metastatic prostate cancer (45 patients)
- 100mer MUC1 peptide, GM-CSF and Poly-ICLC
- 2008-present: Phase II/III in colon cancer prevention (~60 patients with a history of advanced adenomas)
- 100mer MUC1 peptide plus Poly-ICLC adj

### Invention 2: Cyclin B1 Vaccines for Therapy and Prevention of Cancer

- Abnormal Cyclin B1 expression on many different adenocarcinomas and premalignant lesions.
- Immune response against abnormally expressed Cyclin B1 elicited through vaccination controls tumor growth without autoimmunity.
- Clinical trials of vaccines with synthetic cyclin B1 peptides are planned for Stage IB and Stage II lung cancer.
- Cyclin B1 can be a marker of premalignant lesions.
- Immune response to cyclin B1 can be a prognostic marker following diagnosis of lung cancer.

### Proposed Clinical Gene Therapy Using These Lentiviral Vectors (LVs) against MUC1+ Tumors

- Adaptive transfer of T cells engineered to express scTCR by lentiviral vectors
- Transplantation of lentiviral vector transduced hematopoietic stem cells to repopulate the entire immune system
- In vivo delivery of direct iv injection
- Local delivery of LVs into bone marrow chambers

While vaccines provide a non-toxic, practical and cost-effective immunotherapeutic approach to prevention of cancer or treatment of early disease, other forms of immunotherapy can target late disease. The MUC1 specific TCR described above is designed for patients with late stage cancer who have failed other forms of therapy and whose immune system is suppressed by the cancer and previous therapies. This gene therapy/immunotherapy approach is non toxic and expected to be effective long term.