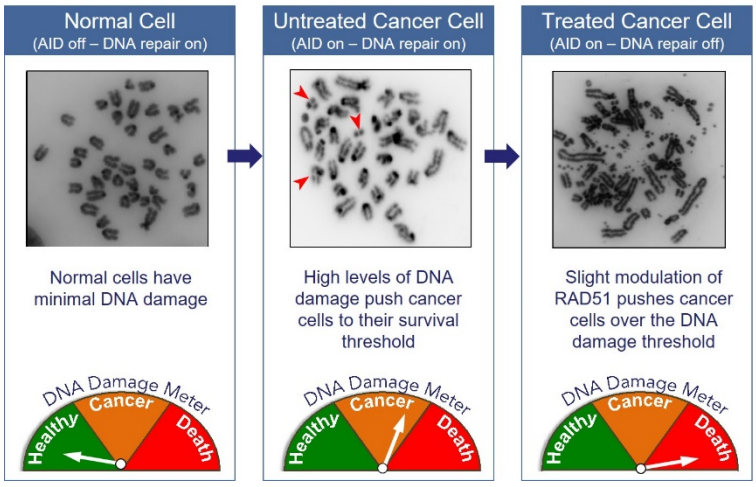
## The Company

Cyteir Therapeutics is a leader in the discovery and development of novel therapeutics based on the biology of DNA repair and synthetic lethality for the treatment of cancer and autoimmune diseases. Our initial approach takes advantage of DNA damage overload to induce selective self-destruction of cells by targeting disease-induced RAD51 transport.

## Therapeutic Approach

Genomic instability is caused by an imbalance between DNA damage and DNA repair and is a key driver of many disease states, but also represents a crucial vulnerability in cancer and autoimmune cells.

Normal cells have very little DNA damage and have sufficient repair capacity to handle it. Diseased cells suffer an excess of DNA damage and thus are extremely sensitive to small perturbations in their DNA repair capacity. By modulating repair slightly, the diseased cell is overwhelmed by its own DNA damage and undergoes cell death ("Synthetic lethality").




Precision modulation of DNA repair proteins in biomarker-defined diseases promises to deliver potent and highly selective therapeutic effects while potentially resulting in far fewer side effects than traditional chemotherapy by precisely targeting diseased cells, maintaining integrity of healthy cells in the process.

## Modulation Over Inhibition: Small molecules that selectively target cells defined by the AID biomarker

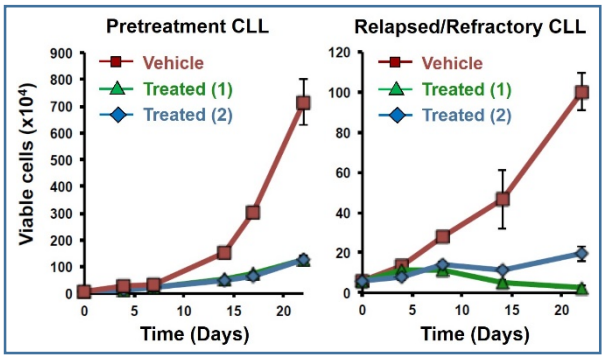
Cyteir's small molecule modulators are selective for disease-causing cells associated with AID, a DNA-damaging enzyme normally present in a very small fraction of healthy immune cells. AID is 'hyperactivated' in many cancers, which accelerates tumor progression and therapy resistance; in many autoimmune diseases, AID hyperactivation also results in the production of high-affinity autoantibodies. DNA repair via the protein RAD51 protects diseased cells and tissues from death by AID-generated DNA damage. Cyteir's modulators restrict the effect of RAD51, resulting in selective self-destruction of diseased cells by way of their own increased genomic instability or synthetic lethality.

## Targeting Genetic Co-dependencies: A novel screening approach for DNA repair drug discovery

Cyteir has developed a unique screening system designed to rapidly identify novel DNA repair modulators that function with exceptional selectivity against biomarker-defined diseased tissues. This screening system utilizes primary cells derived from tissues of interest rather than traditional cell lines. Genetic constraints are then engineered into the cells, which enhances the power to detect hits on the desired pathway. The power of this integrated platform is the robust ability to customize it for any tissue or disease of interest, to rapidly sort out the "true hits" from the false positives and negatives, and to dramatically reduce the failure rate at later stages due to "poor hits" from a physiologically irrelevant screen.

## Programs

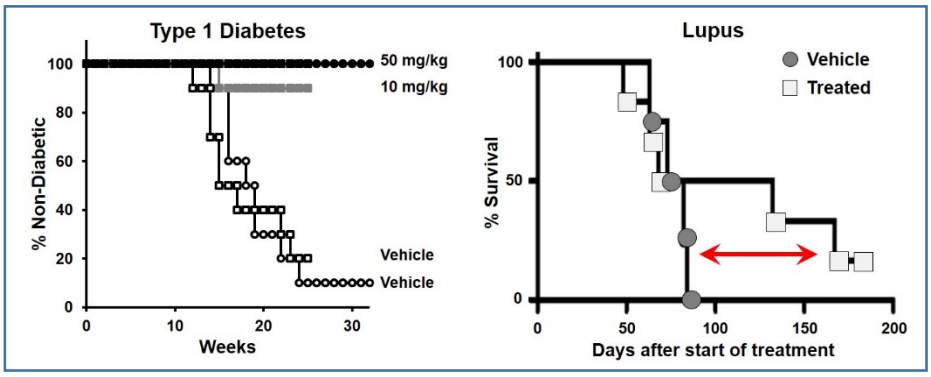
**Oncology**: The biomarker activation-induced cytidine deaminase (AID) is involved in numerous hematological malignancies including non-Hodgkin lymphoma (NHL) and chronic lymphocytic leukemia (CLL) and in solid tumors such as gastric and lung cancer.




Our studies demonstrate that RAD51 modulation is effective against treatment-naïve and relapsed/refractory CLL cells and *in vivo* testing has shown effective tumor reduction with minimal side effects in leukemia and lymphoma xenograft models. Targeting the pathways relevant to genomic instability has significant potential as single agent or combination therapies, and we are exploring combinations with a range of experimental or approved therapeutic agents and approaches.

**Autoimmunity**: Emerging science demonstrates that AID is involved in variety of immune disorders, including autoimmune diseases such as Type I Diabetes (T1D) and Lupus (SLE).

*In vivo* studies show that RAD51 modulation effectively targets AID$^+$ disease-mediating cells, effectively blocking the progression of T1D and SLE with no overt side effects. Our latest data suggest a highly novel immunomodulatory effect that may contribute to stable, long-term disease suppression, which has potential applications for other autoimmune disorders including rheumatoid arthritis, multiple sclerosis, and inflammatory bowel disease.




**New Targets:** There are many kinds of genomic instability in cancer and autoimmunity which result from distinct forms of DNA damage that possess different underlying repair mechanisms. Each of these represents a potential target and forms the basis for sustaining a discovery and product engine using our technological capabilities.

## Key Publications


1. Hasham, MG, et al. Widespread genomic breaks generated by activation-induced cytidine deaminase are prevented by homologous recombination. *Nat Immunol*. 2010 Sep;11(9):820-6.
2. Lamont, KR, et al. Attenuating homologous recombination stimulates an AID-induced antileukemic effect. *J Exp Med*. 2013 May;210(5):1021-33.
3. Ward, A, et al. Targeting homologous recombination, new pre-clinical and clinical therapeutic combinations inhibiting RAD51. *Cancer Treat Rev*. 2015 Jan;41(1):35-45.


## Management Team:

**Donald F. Corcoran**
President & CEO

**Kevin Mills, Ph.D.**
Chief Scientific Officer

**Ron Goldstein, CPA**
Chief Financial Officer

**Joseph Vacca, Ph.D.**
Acting Head of Chemistry

**Darryl Patrick, D.V.M., PhD.**
Acting Head of Preclinical R&D

## Board of Directors:

**Barry Mills, Ph.D., J.D.**
Former President, Bowdoin College

**Donald F. Corcoran**
President & CEO, Cyteir

**Timothy Romberger**
Co-Founder, Cyteir

**Kevin Mills, Ph.D.**
CSO, Cyteir

**Markus Renschler, M.D.**
SVP, Celgene Corporation

## Financing:

**Series A: $5.6M**

**NIH STTR Grant: $2.0M**

**Series B: anticipated Q2 201**

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