Quintessence Biosciences

Quintessence Biosciences, Inc. is a private, clinical stage biopharmaceutical company developing novel anti-cancer compounds based on our patented EVade™ Ribonuclease technology. One of the lead candidates, QBI-139, is in a Phase I trial for solid tumors. Quintessence has a number of opportunities for internal and collaborative development.

Quintessence Biosciences’ EVade™ Ribonuclease technology is covered by patents licensed exclusively to the Company by the Wisconsin Alumni Research Foundation (WARF). Additional intellectual property created within the Company is being secured through the filing and prosecution of additional patents. The Company holds a very strong patent position on the use of ribonucleases for therapeutic applications.

RNA as a Drug Target in Oncology

Traditional small molecule chemotherapies attack DNA in rapidly dividing cells while newer, more cancer-specific therapies are directed to protein targets. The broad efficacy of chemotherapy agents has allowed this class of drugs to remain in many standard of care regimens. However, chemotherapies have highly toxic side-effects and cancer cells can develop a resistance to these chemotherapies, ultimately making them ineffective. Targeted therapies provide benefit with significantly less toxicity, however many of these agents work in only a small subset of patients.

RNA, the mediator between DNA and proteins, has recently been recognized to play a significant role in controlling protein expression.

“RNA as a drug target is appealing since there is the potential to target both proteins and messenger RNA. RNA is also not subject to repair mechanisms and is more accessible than nuclear DNA.”

—National Cancer Institute

EVade™ Ribonuclease Technology

Quintessence Biosciences has transformed ubiquitous ribonucleases, enzymes that degrade RNA, into novel cancer therapeutics. This new family of anti-cancer proteins, called the EVade™ Ribonuclease (RNases), have been engineered to evade the native ribonuclease inhibitor.

- EVade™ RNases kill cancer cells by a novel mechanism — destruction of RNA.
- EVade™ RNases are unlikely to be antigenic in humans.
- The efficacy of the EVade™ RNases is unlikely to be curtailed by efflux pumps.
Pipeline Highlights

**QBI-139: Lead candidate in Phase I Trial—Cancer**

QBI-139 is a variant of human pancreatic RNase 1 that retains 95% sequence identity to the native protein, yet is able to kill cancer cells. QBI-139 has demonstrated significant efficacy in a variety of *in vivo* cancer models, including non-small cell lung, prostate, pancreatic and ovarian cancers. A Phase I trial of QBI-139 in refractory patients with solid tumors is ongoing. Partners for the next stage of clinical trials are being evaluated.

A compound in the same class of drugs (RNases) as QBI-139 is a frog RNase called Onconase. Onconase treatment has led to clinical responses in trials of breast, prostate, non-small cell lung and mesothelioma cancers. The company developing Onconase (Alfacell Corp.) has indicated an NDA will be filed in 2009 for treatment of malignant mesothelioma.

QBI-139 has a number of advantages relative to Onconase, including substantially less toxicity across all species. The doses used at various stages of development of the ribonuclease Onconase are provided. Renal toxicity is dose limiting for Onconase in human clinical trials. The starting dose for QBI-139 in the Phase I trial is more than six-fold higher than the final clinical dose of Onconase.

**PK Enhanced EVade™ RNases—Cancer**

The advantages of the Evade RNases may be enhanced by conjugation to polyethylene glycol (PEG). A family of conjugates is being investigated. One of these compounds is expected to advance to non-clinical studies in 2009.

**Targeted EVade™ RNases—Cancer**

The Evade™ RNases provide a novel alternative to highly toxic small molecule drugs and the non-human protein toxins that are typically targeted using cancer-specific targeting agents, such as antibodies. QBI-139 has a good safety profile relative to both of these classes of drugs, however QBI-139 is an enzyme that can catalyze reactions leading to cell death within the cell. Partners are currently being sought for joint development in this area.

**EVade™ RNases— Infectious Diseases**

Ribonucleases have demonstrated antiviral activity against RNA viruses, including hepatitis and HIV.