While most cancers have decreased, the incidence of deaths from endocrine cancers has increased dramatically. Specifically, adrenal cancers are extremely challenging to successfully treat because of a lack of durable therapies and significant drug toxicities. New treatments are needed to help patients lead longer, healthier lives.

The Solution

University of Michigan Medical School faculty Mark Cohen, M.D. and College of Pharmacy faculty Anna Schwendeman, Ph.D., took a unique approach to addressing this problem. Dr. Cohen developed a lead compound with potent selectivity against human adrenocortical cancers based on his studies of novel natural and semi-synthetic withanolide compounds from the native Physalis plant. But the compound had challenges with drug solubility and circulation half-life, as well as targeting the tumor cells.

To improve the pharmaceutical potential of these withanolides, Cohen and Schwendeman collaborated to develop Scarab, a novel nanoparticle-conjugate using a patented HDL-nanoparticle delivery platform that targets the SR-B1, also known as Scarab 1, receptor on cells.

Results show the ability to deliver withanolide to tumors high in SR-B1 such as adrenal malignancies, while minimizing the toxicity and side effects to other parts of the body.
New endocrine cancer treatment offers improved drug potency and minimal toxicity through a novel combination of HDL nanoparticle and naturally-derived drug compound that selectively targets SR-B1 cancer cell receptors.

**Significant Need**
It is a difficult challenge to effectively treat malignancies of endocrine system organs. Scarab offers a novel drug that is selective against adrenocortical carcinomas (ACCs), carries a better safety and tolerability profile, and has more durable efficacy than current standard of care. In addition, the HDL-nanoparticle delivery platform improves the effectiveness of the withanolides.

**Compelling Science**
Combining a novel naturally-derived withanolide with a patented HDL-nanoparticle delivery platform improves drug delivery and potency.

**Competitive Advantage**
The current standard of care lacks durable efficacy and often limits dosing because of possible drug toxicity issues. Scarab shows highly favorable safety profiles in pre-clinical studies.

**MTRAC Project Key Milestones**
- Optimization, analytical characterization and stability testing of the HDL-TA-WGA particle
- Non-GLP pharmacokinetics and MTD testing
- In vitro drug uptake and cytotoxicity studies in cancer vs. normal cells
- Non-GLP efficacy and drug distribution imaging in ACC xenografts (metastatic disease tumor model)
- Optimization, analytical characterization and stability testing of the HDL-TA-WGA particle
- Non-GLP efficacy and drug distribution imaging in ACC xenografts (solid tumor model)
- Non-GLP single dose toxicology and histology studies

**Overall Commercialization**

**Commercialization Strategy**
License withanolide to a major pharmaceutical company, with ongoing validation of synthetic development.

**Regulatory Pathway**
Accelerate clinical trial entry by utilizing an orphan drug Investigational New Drug (IND) pathway. Demonstrate efficacy and toxicology profile.

**Product Launch Strategy**
Start a biotechnology company that will license Scarab — the final product launch would be determined by licensee.

**Intellectual Property**
Invention disclosure filed — additional patents to be filed.