

# **Press Release**

## FOR IMMEDIATE RELEASE

# CRITICAL OUTCOME TECHNOLOGIES ANNOUNCES IMPORTANT NEW MECHANISM OF ACTION DATA FOR COTI-2

# **Effective in Cell Lines with Mutations in Cancer Suppressing Gene P53**

London, Ontario (September 20, 2012): Critical Outcome Technologies Inc. (COTI) (TSX Venture: COT) announced today new data that broadens the mechanism of action (MOA) of the Company's lead oncology asset, COTI-2, beyond AKT inhibition. Previous preclinical MOA work on COTI-2 clearly showed that COTI-2 modulated the PI3K/AKT/mTOR pathway. However, new data derived from gene profiling and *in vitro* testing with COTI-2 indicates that the drug is particularly effective in treating cancer cell lines with p53 mutations, an effect that is not associated with AKT inhibitors.

"The effectiveness of COTI-2 based on the status of p53, a tumor suppressing gene, could make this compound and class an important new treatment for cancer, as at least 50% of human cancers harbor a p53 mutation," said Dr. Wayne Danter, President and CEO of COTI. "These findings improve our understanding of COTI-2's MOA and help clarify some of the positive results we have seen in earlier experiments and trials that were not explained by AKT inhibition alone."

COTI-2 has a chemical structure that puts it in a class of compounds referred to as thiosemicarbazones. The recognized class effects of thiosemicarbazones include metal ion chelation, the generation of reactive oxygen species (ROS), cancer cell apoptosis and, most recently, the ability to convert certain specific and common p53 mutations to wild type configuration with normal tumor suppressing function. Results from multiple animal models of human cancers indicate that these "class effects" of COTI-2, a third generation thiosemicarbazone, are central to understanding the outcome of these experiments in the context of their potential therapeutic implications.

The detailed analysis of COTI-2's gene profile and the *in vitro* test data produced the following results:

- (1) Multiple genes directly involved with metal binding and programmed cancer cell death were turned on, which is consistent with the known effects of this class of drugs.
- (2) COTI-2 was confirmed to bind to iron in a cell free assay, a common attribute of this class of compounds that leads to programmed cancer cell death.
- (3) The data obtained for 40 human cell lines revealed, in a detailed statistical analysis, that the presence of any p53 mutation strongly predicted cancer cell sensitivity at a very low concentration of COTI-2.

(4) A simple and accurate exploratory predictive model of the relationship between p53 mutation status and COTI-2 *in* vitro activity was created using the currently available test data. This result suggests the p53 gene mutation status might be used to identify which cancers would be most responsive to COTI-2.

#### **Notice to Readers**

Information provided in this press release may contain certain statements which constitute "forward-looking statements" within the meaning of the Securities Act (Ontario) and applicable securities laws. For example, the statement "The effectiveness of COTI-2 based on the status of p53, a tumor suppressing gene, could make this compound and class an important new treatment for cancer" is a forward-looking statement. This statement conveys the Company's belief in COTI-2's ability to make it into and through clinical trials and to the market as a cancer treatment, but COTI is not in a position at this time to determine when and if COTI-2 will ever enter the market. Forward-looking statements, by their nature, are not guarantees of future performance and are based upon management's current expectations, estimates, projections and assumptions. Risks that could impact on these forward-looking statements are outlined in the Company's annual information form. Management of COTI considers the assumptions on which these forward-looking statements are based to be reasonable, but as a result of the many risk factors, cautions the reader that actual results could differ materially from those expressed or implied in these forward-looking statements.

### **About Critical Outcome Technologies Inc.**

COTI is a leading-edge company specializing in accelerating the discovery of small molecules thus enabling these new drugs to be brought to market in a more cost effective, efficient and timely manner. COTI'S proprietary artificial intelligence system, CHEMSAS®, utilizes a series of predictive computer models to identify compounds with high probability of being successfully incorporated in disease-specific drug discovery, as well as subsequent optimization and preclinical development. These compounds are targeted for a variety of diseases, particularly those for which current treatments are either lacking or ineffective.

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