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**Diazon Pharmaceutical's anti-cancer agent DZ-2384 mechanism for high activity and low neurotoxicity published by McGill researchers in *Science Translational Medicine***

Montreal, QC, November 16th 2016 – [Diazon Pharmaceuticals Inc.](#) today announced the publication of a preclinical oncology study identifying the novel mechanism of action of its new synthetic diazonamide compound, DZ-2384, in *Science Translational Medicine*. The results show that a distinct mode of binding to a classic therapeutic site in tubulin translates into superior anti-tumor activity and safety, including lack of neurotoxicity, with pre-clinical proof of concept in a wide range of cancers including triple-negative breast cancer and pancreatic cancer.

The study, titled "The synthetic diazonamide DZ-2384 has distinct effects on microtubule curvature and dynamics without neurotoxicity," by Michal Wieczorek et al., highlights distinct structural features of DZ-2384 binding to tubulin that help preserve the cell microtubular infrastructure of neurons and non-dividing cells, resulting in lower toxicity. DZ-2384's novel mechanism of action was shown to result in unique effects on microtubule curvature and dynamics distinct from other agents in its class.

Anti-mitotic tubulin-binding agents constitute part of the standard-of-care in over 15 different oncology indications. Treatment is accompanied by significant toxicities including neurotoxicity that often limit their use and effectiveness. In contrast, DZ-2384 did not cause peripheral neuropathy at efficacious doses, yet retained potent activity in preclinical models.

Diazon partnered with the [Laboratory for Therapeutic Development](#) at the Rosalind and Morris Goodman Cancer Research Center, McGill University to elucidate DZ-2384's mechanism of action and to determine which cancers are likely to derive the most therapeutic benefit from this agent. The research was led by Drs. Anne Roulston and Gordon Shore of the Laboratory for Therapeutic Development and Dr. Gary Brouhard at the University's Department of Biology and included several international collaborators.

**Robert G. McNeil, Ph.D., chairman of the board of directors of Diazon,** said "Anti-mitotic agents represent the bedrock standard-of-care for thousands of cancer patients worldwide. Their narrow safety margin, including high incidences of peripheral neuropathy, severely restrict their utility. The positive results of both drug efficacy and toxicity studies leads us to believe that DZ-2384 has a wide safety margin with the potential to treat a substantial patient population across multiple cancer indications. The publication in this prestigious journal emphasizes the importance and timeliness of DZ-2384 in an era of intense interest in safely combining chemotherapy with targeted agents. The findings reinforce our expectations that DZ-2384 will present a significant improvement in the treatment of multiple cancers."

**Anne Roulston, Ph.D., associate director of the Laboratory for Therapeutic Development at the Goodman Cancer Research Center, McGill University,** said "The data provide us with key insights into the basic attributes of DZ-2384 and demonstrate preclinical proof of its validity as a new generation of



chemotherapy. Such a drug could be used both as sole treatment or in combination with other therapies, such as immuno-oncology. We believe DZ-2384 has the potential to be a highly effective and safer alternative to current anti-mitotic agents.”

For more information about DZ-2384 and Diazon Pharmaceuticals Inc. please visit <http://www.diazonpharmaceuticals.com/>

#### **About DZ-2384**

DZ-2384 is a pre-clinical, optimized and commercially scalable synthetic derivative of Diazonamide A that exhibits potent anti-tumor activity in models of multiple cancer types. It is an anti-mitotic drug that has high safety margin and lacks neurotoxicity in rats at effective plasma levels. DZ-2384 binds the vinca domain of tubulin in a distinct way, imparting structurally and functionally different effects on microtubule dynamics compared to other vinca binding compounds. Binding results in unique effects on microtubule curvature, translating into mechanisms that preserve the microtubule integrity of neurons and non-dividing cells, compared to current anti-mitotic drugs. DZ-2384 is being developed by Diazon Pharmaceuticals to become the new chemotherapy standard of care in multiple oncology indications.

#### **About anti-mitotic drugs**

Chemotherapy drugs target cells at different phases of the process of forming new cells. Cancer cells tend to form new cells more quickly than normal cells and this makes them a better target for chemotherapy drugs. One family of commonly used chemotherapies, known as anti-mitotic drugs, are agents that disrupt mitotic spindle assembly. Traditional anti-mitotic agents include the microtubule toxins such as paclitaxel (Taxol), other taxanes and the vinca alkaloids, all of which have proven successful in the clinic. However, patient response remains highly unpredictable, and drug resistance is common. In addition, toxicity is a major problem.

#### **About Diazon Pharmaceuticals Inc.**

Diazon Pharmaceuticals, a Montreal based company, is developing the onco-therapeutic DZ-2384 that targets a proven therapeutic pathway in oncology, but one whose potential in modern cancer therapy has been severely restricted due to unacceptable toxicities. DZ-2384 overcomes this restriction by modulating microtubule structure and dynamics in a distinct way, delivering potent anti-tumor efficacy with a superior safety profile. The company was founded in 2013 by researchers at UCLA and McGill University.

#### **About the Laboratory for Therapeutic Development at the Goodman Cancer Research Center, McGill University ([www.ltdmcgill.ca](http://www.ltdmcgill.ca))**

The Laboratory for Therapeutic Development (LTD) was created in 2010 by Dr. Gordon Shore and Dr. Anne Roulston as part of the Rosalind and Morris Goodman Cancer Research Centre (GCRC) and Department of Biochemistry at McGill University. The LTD was established to discover biomarkers and clinical strategies for the most effective use of various anti-cancer compounds using a platform in functional genomics. The LTD was initially funded through research grants from the Québec Consortium for Drug Discovery (CQDM) and Génome Québec (GQ), with all equipment donated by Cephalon.



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