Rakovina Therapeutics Announces Publication Highlighting Activity of Novel Bi-functional PARP-HDAC Inhibitor in Preclinical Models of Ewing Sarcoma

Publication to be available on pre-print server, bioRxiv, and will be submitted for scientific journal peer-review

VANCOUVER, BC, November 14, 2022 /CNW/ – Rakovina Therapeutics Inc. (TSX-V: RKV) ("the Company"), today announced publication of a scientific article on the anti-cancer activity of the Company's novel dual PARP-HDAC inhibitor in models of Ewing sarcoma.

The manuscript entitled "A bi-functional PARP-HDAC inhibitor with activity in Ewing sarcoma", indicate a benefit of dual PARP and HDAC inhibition and provide proof-of-concept for a bi-functional single-molecule therapeutic strategy in the treatment of Ewing sarcoma.

Ewing sarcoma is a highly aggressive bone and soft tissue tumor affecting mainly children and young adults, with a dismal 5-year survival rate of 15-30% for metastatic disease. Previous studies have demonstrated that Ewing sarcoma cells are sensitive to FDA-approved PARP inhibitors, but clinical trials have failed to produce a durable treatment response.

PARP inhibitors have been demonstrated to impact tumors that harbor BRCA mutations or other defects in homologous repair (HR). This concept is commonly referred to as "BRCAness".

Ewing sarcoma is characterized by the presence of a genetic fusion involving the EWSR1 gene. This fusion has been shown to impair HR activity indicating a level of "BRCAness" in Ewing sarcoma. The lack of clinical response in Ewing sarcoma to treatment with single-agent PARP inhibitors supports employing combination therapy strategies that further inhibit HR and increase BRCAness in Ewing sarcoma.

Recent studies in leukemia, breast cancer, liver cancer, glioblastoma, prostate cancer and anaplastic thyroid models demonstrated suppression of HR following treatment with HDAC inhibitors, supporting the synergistic potential of dual HDAC and PARP inhibition.

Rakovina Therapeutics researchers characterized and tested kt-3283, a novel dual-function single molecule of PARP and HDAC in Ewing sarcoma model systems. In these studies, kt-3283 demonstrated higher efficacy than treatment with single-agent PARP or HDAC inhibitors. These data indicate the dual activity of kt-3283 is 30- to 80-times more potent in Ewing sarcoma models than an FDA-approved PARP inhibitor, and 30- to 60-times more potent than an FDA-approved HDAC inhibitor. In an Ewing sarcoma metastasis model, kt-3283 prevented metastatic cancer growth in the lungs of mice inoculated with an aggressive Ewing sarcoma cell line.

"These results provide proof-of-concept for a novel single-molecule PARP-HDAC inhibitor in the treatment of Ewing sarcoma," stated Prof. Mads Daugaard Rakovina Therapeutics' president and chief scientific officer. "This concept will likely be relevant in other cancer indications beyond Ewing sarcoma and potentially offer an opportunity to suppress therapeutic resistance to PARP-inhibitor treatment."

Development of Rakovina Therapeutics' novel kt-3000 DNA-damage response inhibitors is supported, in part, by the St. Baldrick's Foundation Martha's BEST Grant for All, which is

aimed at developing new treatments for Ewing sarcoma, an aggressive bone and soft tissue cancer in children and young adults.

About Rakovina Therapeutics Inc.

Rakovina Therapeutics Inc. is focused on the development of new cancer treatments based on novel DNA-damage response (DDR) technologies. The Company has established a pipeline of novel DNA-damage response inhibitors with the goal of advancing one or more drug candidates into human clinical trials and obtaining marketing approval for new cancer therapeutics from Health Canada, the United States Food and Drug Administration and similar international regulatory agencies. Further information may be found at www.rakovinatherapeutics.com.

Additional Information

The TSXV has neither approved nor disapproved the content of this press release. Neither the TSXV nor its Regulation Services Provider (as that term is defined in policies of the TSXV) accepts responsibility for the adequacy or accuracy of this release.

Notice regarding forward-looking statements:

This release includes forward-looking statements regarding the Company and its respective business, which may include, but is not limited to, statements with respect to the proposed business plan of the Company and other statements. Often, but not always, forward-looking statements can be identified by the use of words such as “plans”, “is expected”, “expects”, “scheduled”, “intends”, “contemplates”, “anticipates”, “believes”, “proposes” or variations (including negative variations) of such words and phrases, or state that certain actions, events, or results “may”, “could”, “would”, “might” or “will” be taken, occur or be achieved. Such statements are based on the current expectations of the management of the Company. The forward-looking events and circumstances discussed in this release may not occur by certain specified dates or at all and could differ materially as a result of known and unknown risk factors and uncertainties affecting the Company, including risks regarding the medical device industry, economic factors, regulatory factors, the equity markets generally and risks associated with growth and competition. Although the Company has attempted to identify important factors that could cause actual actions, events, or results to differ materially from those described in forward-looking statements, there may be other factors that cause actions, events, or results to differ from those anticipated, estimated or intended. No forward-looking statement can be guaranteed. Except as required by applicable securities laws, forward-looking statements speak only as of the date on which they are made and the Company undertakes no obligation to publicly update or revise any forward-looking statement, whether as a result of new information, future events, or otherwise. The reader is referred to the Company’s most recent filings on SEDAR for a more complete discussion of all applicable risk factors and their potential effects, copies of which may be accessed through the Company’s profile page at www.sedar.com.

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