Publication in *The New England Journal of Medicine* Confirms that Tens of Thousands of Women with Node-positive, Early-stage Breast Cancer Can Avoid Chemotherapy with the Oncotype DX® Test

- **RxPONDER, an independent study led by SWOG Cancer Research Network, demonstrates that guiding treatment with Oncotype DX test can spare chemotherapy use in majority of postmenopausal women**
- **Results have already led to updated NCCN Guidelines® for breast cancer**
- **New RxPONDER results to be featured in oral presentation at 2021 San Antonio Breast Cancer Symposium (SABCS)**

LONDON, December 2, 2021 – Exact Sciences Corp. (NASDAQ: EXAS) today announced that data from the **Rx** for **Po**sitive **No**d**e**, **E**ndocrine **R**esponsive Breast Cancer, or RxPONDER, trial were published in *The New England Journal of Medicine*.[i] The study, led by the independent SWOG Cancer Research Network and sponsored by the National Cancer Institute (NCI), successfully defined the benefit of chemotherapy in early-stage, node-positive breast cancer patients with Oncotype DX Breast Recurrence Score® results of 0 to 25. Initial results from RxPONDER were reported at the 2020 San Antonio Breast Cancer Symposium (SABCS). The findings have now been confirmed in this peer-reviewed publication.

In the study, postmenopausal women with 1 to 3 positive nodes and Recurrence Score® results of 0 to 25 showed no benefit from chemotherapy after a median of five years of follow-up, meaning they can potentially avoid negative side effects of the treatment. Importantly, no chemotherapy benefit was observed regardless of the number of affected nodes, tumor grade or size. In premenopausal women with 1 to 3 positive nodes, a statistically significant chemotherapy benefit was observed.

Approximately one-third of patients diagnosed with hormone receptor (HR)-positive, HER2-negative early breast cancer have a tumor that has spread to their lymph nodes. The vast majority of these patients currently receive chemotherapy[ii] even though approximately 85% of them have Recurrence Score results of 0 to 25.[iii] In addition, approximately two out of three early-stage breast cancer patients are postmenopausal.[iv]

“The RxPONDER publication demonstrate practice-changing results which show that postmenopausal women with this common form of breast cancer and a RS 0-25 can be spared unnecessary chemotherapy and receive only hormone therapy, potentially saving many women the time, and harmful side effects that can be associated with chemotherapy. For the

premenopausal women diagnosed with breast cancer who may benefit from chemotherapy, the data could help individualise the discussion of risk and benefit of chemotherapy." Said **Professor Mark Beresford, Consultant Clinical Oncologist and Clinical Lead at the Royal United Hospital Bath**

"At present in the UK, most women with breast cancer which has spread to the lymph nodes will be advised to consider chemotherapy. RxPONDER is an independently conducted trial of a very large number of women with involved lymph nodes who were tested using the Oncotype DX® test. The results show that the test can distinguish a majority of postmenopausal women who can safely avoid chemotherapy. This will come as a great reassurance to these women (and their treating clinicians) that they can confidently avoid the risks, economic impact and rigours of chemotherapy," said **Mr. Simon Holt, Honorary Consultant Surgical Oncologist at Hywel Dda University Hospital and Chief Investigator** of the ongoing study into the impact of the Oncotype DX® test on treatment decisions in node-positive early breast cancer patients in the UK.

Based on the RxPONDER results, the National Comprehensive Cancer Network® (NCCN®)[v] updated its guidelines for breast cancer and recognised the Oncotype DX Breast Recurrence Score test as the only test that can be used for prediction of chemotherapy benefit in early-stage breast cancer patients with 1 to 3 positive axillary lymph nodes, including micrometastases.[vi] The Oncotype DX test is now the only test classified as "preferred" with the highest level of evidence for node-negative and postmenopausal node-positive (1 to 3 positive nodes) patients. In addition, NCCN recommends considering the test to assess prognosis in premenopausal node-positive patients who are candidates for chemotherapy.

"The RxPONDER results, together with the foundational TAILORx results[vii] in node-negative, early-stage breast cancer, further elevate the test to a standard of care, supporting its inclusion in guidelines as well as its reimbursement and adoption on a global scale," said **Rick Baehner, M.D., chief medical officer of Precision Oncology at Exact Sciences**. "Now with the RxPONDER results, many more women worldwide may be able to receive hormone therapy alone, avoiding the negative side effects of chemotherapy without increasing the risk of cancer returning."

One of the largest clinical trials in node-positive, HR-positive, HER2-negative early breast cancer, RxPONDER enrolled more than 5,000 women with up to three positive nodes. The prospective, randomised Phase III study was conducted at 632 sites in nine countries – the United States, Canada, Mexico, Colombia, Ireland, France, Spain, South Korea and Saudi Arabia. Women with a Recurrence Score result of 0 to 25 were randomised to treatment with hormone therapy alone or chemotherapy followed by hormone therapy. Randomised patients were stratified based on their Recurrence Score result, menopausal status and type of lymph node

surgery. Further analyses and additional patient follow up are planned by the SWOG investigators.

About the Oncotype DX® and Oncotype MAP™ Portfolio of Tests

The Oncotype DX portfolio of breast, colon and prostate cancer tests applies advanced genomic science to reveal the unique biology of a tumour in order to optimize cancer treatment decisions. In breast cancer, the Oncotype DX Breast Recurrence Score test is the only test that has been shown to predict the likelihood of chemotherapy benefit as well as recurrence in invasive breast cancer. Additionally, the Oncotype DX Breast DCIS Score™ test predicts the likelihood of recurrence in a pre-invasive form of breast cancer called DCIS. For patients with advanced and metastatic cancer, the company offers the Oncotype MAP™ Pan-Cancer Tissue test, a rapid, comprehensive tumour profiling panel, which provides results in three to five business days[viii] and allows physicians to understand a patient's tumor profile and recommend actionable targeted therapies or clinical trials. With more than 1 million patients tested in more than 90 countries, the Oncotype DX tests have redefined personalised medicine by making genomics a critical part of cancer diagnosis and treatment. To learn more about the Oncotype DX and Oncotype MAP tests, visit www.oncotypeiq.com/en-GB

About Exact Sciences Corp.

A leading provider of cancer screening and diagnostic tests, Exact Sciences relentlessly pursues smarter solutions providing the clarity to take life-changing action, earlier. Building on the success of the Cologuard® and Oncotype® tests, Exact Sciences is investing in its product pipeline to take on some of the deadliest cancers and improve patient care. Exact Sciences unites visionary collaborators to help advance the fight against cancer. For more information, please visit the company's website at www.exactsciences.co.uk, follow Exact Sciences on Twitter @ExactSciences, or find Exact Sciences on Facebook.

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Forward-Looking Statements

This news release contains forward-looking statements concerning our expectations, anticipations, intentions, beliefs or strategies regarding the future. These forward-looking statements are based on assumptions that we have made as of the date hereof and are subject to known and unknown risks and uncertainties that could cause actual results, conditions and events to differ materially from those anticipated. Therefore, you should not place undue reliance on forward-looking statements. Risks and uncertainties that may affect our forward-looking statements are described in the Risk Factors sections of our most recent Annual Report on Form 10-K and any subsequent Quarterly Reports on Form 10-Q, and in our other reports filed with the Securities and Exchange Commission. We undertake no obligation to publicly update any forward-looking statement, whether written or oral, that may be made from time to time, whether as a result of new information, future developments or otherwise.

[i] Kalinsky K, et al. New Engl J Med. 2021.

[ii] Zhang et al. Breast Can Res Treat. 2020.
[iii] Bello et al. Ann Surg Oncol. 2018.
[iv] Heer E, et al. The Lancet. 2020.
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[vi] Referenced with permission from the NCCN Clinical Practice Guidelines in Oncology (NCCN Guidelines®) for Breast Cancer, V.3.2021©National Comprehensive Cancer Network, Inc. 2021. All rights reserved. Accessed May 17, 2021. To view the most recent and complete version of the guidelines, go online to: https://www.nccn.org/professionals/physician_gls/pdf/breast.pdf.
[vii] Sparano et al. New Engl J Med. 2018.
[viii] Exact Sciences internal data on file. Turnaround time based on qualified sample receipt.