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New Data Presented at SABCS 2021 Strengthen Value of Oncotype DX Breast Recurrence Score® Test to Inform Clinical Decision-making

- **Updated RxPONDER study analysis provides further evidence that the test identifies the majority of women with early-stage, node-positive breast cancer who can avoid chemotherapy**

MADISON, Wis., December 9, 2021 – Exact Sciences Corp. (NASDAQ: EXAS), a global leader in cancer diagnostics, today announced the presentation of new data at the 2021 San Antonio Breast Cancer Symposium® (SABCS®) supporting the clinical value of the Oncotype DX Breast Recurrence Score test. New analyses presented at the meeting include an oral presentation of updated data from the RxPONDER study led by the independent SWOG Cancer Research Network, and sponsored by the National Cancer Institute (NCI).

"New findings presented at SABCS 2021 add to the wealth of data highlighting the role of the Oncotype DX® test in providing critical information to personalize and improve the quality of breast cancer treatment decisions," said Rick Baehner, M.D., chief medical officer of Precision Oncology at Exact Sciences. "Additionally, we are encouraged by results from a study validating our new 16-gene genomic radiation therapy signature in development, showing promise in identifying women with early-stage breast cancer who may be able to forgo irradiation following breast conserving surgery."

New data from RxPONDER confirm and strengthen previous findings
Following the recent publication of initial study results in *The New England Journal of Medicine*[i], updated data were presented in an oral session[ii] at SABCS by Dr. Kevin Kalinsky, study lead investigator. In an analysis with longer follow-up (median 6.1 years), the investigators reported that postmenopausal women with 1-3 positive nodes and Recurrence Score® results 0-25 continue to not benefit from adjuvant chemotherapy. In addition, a new analysis of distant recurrence-free interval (defined as time to distant recurrence or death from breast cancer) showed that premenopausal women with Recurrence Score results 0-13 received a modest 2.3% absolute benefit at five years. For those with Recurrence Score results 14-25 the benefit was 2.8%.

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[iii] even though approximately 85% of them have Recurrence Score results 0 to 25.[iv] In addition, approximately two out of three early-stage breast cancer patients are postmenopausal.[v]

Use of a 16-gene radiation therapy signature to identify patients with HR-positive, HER2-negative early-stage breast cancer who may skip radiotherapy
The study, presented at SABCS in a poster session[vi], applied the 16-gene radiation therapy signature to 132 patients enrolled in the Princess Margaret Trial, which randomized patients ages 50 or older to radiotherapy and tamoxifen or tamoxifen alone after breast conserving surgery. The results, in a treatment cohort in line with the current standard of care, support previous validation study data[vii] suggesting that the 16-gene radiation therapy signature may be used to identify patients with a low risk of locoregional recurrence who will not experience significant benefit from adjuvant radiotherapy. The 16-gene radiation therapy signature was developed by PFS Genomics, a company acquired by Exact Sciences earlier this year.

Additional Oncotype DX data presented at SABCS 2021
Other data featured in Poster Sessions and Spotlight Poster Discussions at SABCS 2021 include the following:

Poster #P1-08-28: Real world use of Oncotype DX testing in the management of breast cancer. The North East England experience
Authors: Gault, A., et al.
Date/Time: Wednesday, December 8, 7:00-9:30 a.m. CT

Poster #P2-15-02: Using Oncotype DX Breast Recurrence Score (RS) assay to define the role of neoadjuvant endocrine therapy (NET) in early-stage hormone receptor positive (HR+) breast cancer (BC)
Authors: Taylor, C., et al.
Date/Time: Wednesday, December 8, 5:00-6:30 p.m. CT

Spotlight Poster #PD9-01: Expanding downstaging criteria in AJCC pathologic prognostic staging using Oncotype DX Recurrence Score assay in T1-2N0 hormone-receptor positive patients enrolled in the TAILORx Trial
Authors: Kantor, O., et al.
Date/Time: Thursday, December 9, 7:00-8:30 a.m. CT

Spotlight Poster #PD15-05: Assessment of estrogen receptor (ESR1) mRNA expression for prediction of extended aromatase inhibitor benefit in HR-positive breast cancer using NRG Oncology/NSABP B-42
Authors: Mamounas, E., et al.
Date/Time: Friday, December 10, 7:00-8:30 a.m. CT

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 tumor 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 risk of distant 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 tumor 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 personalized 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

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.com, follow Exact Sciences on Twitter @ExactSciences, or find Exact Sciences on Facebook.

NOTE: Oncotype, Oncotype DX, Oncotype DX Breast Recurrence Score, Oncotype DX Breast DCIS Score, Recurrence Score and Oncotype MAP are trademarks or registered trademarks of Genomic Health, Inc. Exact Sciences and Cologuard are trademarks or registered trademarks of Exact Sciences Corporation. All other trademarks and service marks are the property of their respective owners.

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. 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.

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[i] Kalinsky, K. et al., New Engl J Med. 2021.
[ii] Kalinsky, K. et al., Oral Presentation: [GS2-07]. San Antonio Breast Cancer Symposium; December 2021.
[iii] Zhang et al., Breast Can Res Treat 2020.
[iv] Bello et al., Ann Surg Ocol. 2018.
[v] Heer E. et al., The Lancet 2020.
[vi] Fyles, A. et al., Poster : [P2-08-01]. San Antonio Breast Cancer Symposium; December 2021.
[vii] Sjöström, M., et al. Abstract #512, ASCO 2021.
[viii] Exact Sciences internal data on file. Turnaround time based on qualified sample receipt.