NEWS RELEASE

# Prospective, Multi-center Study Published in Future Oncology Demonstrates DecisionDx®-Melanoma's i31-SLNB Result Outperforms Staging Criteria in Identifying Patients with Cutaneous Melanoma Below the 5% NCCN Threshold for Forgoing SLNB

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Among all patients studied, 2.6% nodal positivity and 97.8% three-year recurrence-free survival (RFS) was observed in those predicted to have less than 5% risk of a positive sentinel lymph node (SLN) by DecisionDx-Melanoma's i31-SLNB

Only 1.4% SLN positivity was observed in patients with T1b–T2a tumors predicted to have less than 5% risk

The Company will host a webcast on Monday, March 23, at 4:30pm Eastern Time to discuss data from the publication

FRIENDSWOOD, Texas, March 13, 2026 (GLOBE NEWSWIRE) -- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced the publication of results from the largest prospective, multicenter study to date evaluating DecisionDx-Melanoma's integrated sentinel lymph node biopsy (i31-SLNB) test result.[1] The paper, available in **Future Oncology**, confirms that DecisionDx-Melanoma's i31-SLNB identifies patients below the 5% National Comprehensive Cancer Network® (NCCN) threshold for forgoing sentinel lymph node biopsy (SLNB) and outperforms traditional staging criteria and other predictive gene expression profile (GEP) tests.

"What makes these findings meaningful is the clear separation between low- and high-risk patients using

DecisionDx-Melanoma's i31-SLNB," said J. Michael Guenther, M.D., co-author and surgical oncologist at St. Elizabeth Physicians in Edgewood, Kentucky. "When a patient's predicted risk is below 5%, the observed precision of the i31-SLNB gives us great confidence that forgoing SLNB is appropriate, while still maintaining excellent outcomes for our patients. Conversely, patients predicted to have a greater than 10% likelihood of a positive SLN by the i31-SLNB had an actual SLN positivity rate of 21.4% — more than eight times higher than those predicted to have a low likelihood of a positive SLN."

Current NCCN Cutaneous Melanoma (CM) Guidelines recommend forgoing SLNB when the likelihood of SLN positivity is less than 5%, considering SLNB when risk is between 5–10% and offering the procedure when risk exceeds 10%. DecisionDx-Melanoma's i31-SLNB integrates the independently validated 31-GEP score with established clinicopathologic factors, including Breslow thickness, ulceration, mitotic rate and age, to generate a personalized likelihood of SLN positivity that supports decision-making aligned with these guideline thresholds.

In this prospective, multicenter study of 912 patients with T1–T4 cutaneous melanoma enrolled across 30 U.S. centers, 430 patients underwent SLNB and 482 did not, allowing for evaluation of both nodal positivity and recurrence outcomes.

Among patients who underwent SLNB:

- Patients with less than 5% predicted risk of SLN positivity by DecisionDx-Melanoma's i31-SLNB had an actual SLN positivity rate of 2.6%.
- Patients with greater than 10% predicted risk had an SLN positivity rate of 21.4%, an 8.2-fold greater likelihood.

In early-stage disease where SLNB decision-making is often most nuanced:

- Among patients with T1–T2a tumors, SLN positivity was only 1.8% in those with an i31-SLNB less than 5% predicted risk.
- In contrast, SLN positivity was 16.7% in those with greater than 10% predicted risk by i31-SLNB, a 9.3-fold greater likelihood.

All patients with a low-risk i31-SLNB result (less than predicted 5% risk) who had at least two years of follow up (or a recurrence) demonstrated a 97.8% three-year RFS rate, indicating a very low risk of recurrence.

Beyond nodal positivity rates, the study also evaluated performance relative to established guideline benchmarks and other predictive tests. Table 3 from the manuscript (available here) reports true-negative to false-negative

(TN:FN) ratios comparing the standard established by NCCN guidelines which uses American Joint Committee on Cancer (AJCC) staging criteria, DecisionDx-Melanoma's i31-SLNB and other predictive gene expression profile tests, (i.e., CP-GEP), across tumor stages.

A TN:FN ratio of 19:1 corresponds to a 5% miss rate, meaning that for every 19 true-negative SLNBs, one positive SLNB would have been missed, consistent with NCCN guideline thresholds. Ratios greater than 19:1 indicate performance exceeding AJCC/NCCN guidance, while ratios below 19:1 indicate higher miss rates.

In this study, the i31-SLNB demonstrated a TN:FN ratio of 55:1 in T1–T2a patients and 73:1 in the clinically important T1b–T2a subgroup, exceeding the 19:1 guideline benchmark. By comparison, previously reported data for other predictive GEP tests, including CP-GEP in T1–T2 disease, have shown lower TN:FN ratios (15:1). These findings highlight the ability of the i31-SLNB to more precisely identify patients at low risk of SLN positivity while minimizing missed positive nodes, particularly in early-stage tumors where accurate identification below the 5% threshold is critical to avoid unnecessary procedures.

Overall, the published data confirm that DecisionDx-Melanoma's i31-SLNB can identify patients at sufficiently low risk of nodal positivity to safely forgo SLNB, reducing unnecessary procedures, procedure-related complications and healthcare costs while supporting risk-aligned management.

Webcast Details
The live webcast will take place on March 23, 2026, at 4:30 p.m. Eastern Time and can be accessed here: **https://events.q4inc.com/attendee/394408771**, or via the webcast link on the Investor Relations page of the Company's website: **https://ir.castlebiosciences.com/overview/default.aspx**. A replay of the webcast will be available following its conclusion.

Speaker details:
J. Michael Guenther, M.D., surgical oncologist, St. Elizabeth Physicians, Edgewood, Kentucky

- John Wayne Institute – Fellowship (Santa Monica, CA)
- University of Cincinnati – Residency (Cincinnati, OH)
- University of Michigan Medical School (Ann Arbor, MI)
- American Board of Surgery: General

There will be a brief Question and Answer session following prepared remarks.

About DecisionDx-Melanoma

DecisionDx-Melanoma is a gene expression profile (GEP) test designed to analyze tumor biology to deliver a personalized risk assessment for patients with stage I–III cutaneous melanoma, enhancing risk stratification beyond American Joint Committee on Cancer (AJCC) staging alone. By combining molecular insights with select clinicopathologic features, the test provides two distinct outputs: a personalized risk of sentinel lymph node (SLN) positivity and a personalized risk of recurrence and/or metastasis. This clinically actionable information is designed to help guide risk-aligned patient management decisions, including SLN biopsy consideration, follow-up intensity, imaging and referrals.

DecisionDx-Melanoma is supported by more than 50 peer-reviewed publications, including prospective studies and meta-analyses, and was developed in collaboration with more than 100 leading U.S. institutions. The test has been clinically validated in more than 10,000 patient samples, ordered more than 220,000 times since launch, and has been shown to be associated with improved patient survival. Learn more at **https://castlebiosciences.com/tests/prognostic/decisiondx-melanoma/overview**.

About Castle Biosciences
Castle Biosciences (Nasdaq: CSTL) is a leading diagnostics company improving health through innovative tests that guide patient care. With a primary focus in dermatologic and gastroenterological disease, we develop personalized, clinically actionable solutions that help improve disease management and patient outcomes.

We put people first—empowering patients and clinicians and informing care decisions through rigorous science and advanced molecular tests that support more confident treatment planning. To learn more, visit **www.CastleBiosciences.com** and connect with us on **LinkedIn**, **Instagram**, **Facebook** and **X**.



Forward-Looking Statements
This press release contains forward-looking statements within the meaning of Section 27A of the Securities Act of 1933, as amended, and Section 21E of the Securities Exchange Act of 1934, as amended, which are subject to the "safe harbor" created by those sections. These forward-looking statements include, but are not limited to, statements concerning: the ability of DecisionDx-Melanoma's i31-SLNB test to (i) generate a personalized likelihood of SLN positivity to support risk-aligned shared decision-making consistent with NCCN guideline thresholds; and (ii) reduce unnecessary procedures, procedure-related complications and healthcare costs. The words "designed," "may", "can", and similar expressions are intended to identify forward intentions or expectations disclosed in our forward-looking statements, and you should not place undue reliance on our forward-looking statements. Actual results or events could differ materially from the plans, intentions and expectations disclosed in the forward-

looking statements that we make. These forward looking statements involve risks and uncertainties that could cause actual results to differ materially from those in the forward-looking statements, including, without limitation: subsequent study or trial results and findings may contradict earlier study or trial results and findings or may not support the results obtained in these studies, including with respect to the discussion of our tests in this press release; actual application of our tests may not provide the aforementioned benefits to certain patients; and the risks set forth under the heading “Risk Factors” in our Annual Report on Form 10-K for the year ended December 31, 2025, and our subsequent Quarterly Reports on Form 10-Q, each as filed or to be filed with the SEC, and in our other filings with the SEC. The forward-looking statements are applicable only as of the date on which they are made, and we do not assume any obligation to update any forward-looking statements, except as may be required by law.

1. Beard T, Guenther JM, Leong SP, et al. The integrated 31-gene expression profile test identifies low-risk patients with cutaneous melanoma who can forego the SLNB procedure: results from a prospective, multicenter trial. Future Oncol. Published online [March 13, 2026]. doi: **https://doi.org/10.1080/14796694.2026.2640227**

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