NEWS RELEASE

Data Presentation at 2023 Winter Clinical - Miami™ Highlights Use of DecisionDx®-Melanoma to Guide SLNB Surgery Decisions in Head and Neck Tumors

2/22/2023

Additional presentation on Castle's pipeline test for inflammatory skin diseases highlights unmet clinical need

FRIENDSWOOD, Texas--(BUSINESS WIRE)-- Castle Biosciences, Inc. (Nasdaq: CSTL), a company improving health through innovative tests that guide patient care, today announced that new data on DecisionDx®-Melanoma and the Company's pipeline test for inflammatory skin diseases was presented at the recent 2023 Winter Clinical - Miami™ conference.

The poster presentation for DecisionDx®-Melanoma strengthens the evidence supporting use of the test to provide risk stratification for patients in order to guide risk-appropriate sentinel lymph node biopsy (SLNB) surgery decisions. Additionally, the poster for Castle's inflammatory skin disease pipeline test highlights feedback from clinicians regarding therapy selection strategies, informing the development of Castle's pipeline test and supporting the unmet clinical need for a molecular test to guide therapeutic selection for patients with inflammatory skin diseases.

DecisionDx®-Melanoma

Poster title: The i31-gene expression profile test for cutaneous melanoma identifies patients with head and neck tumors who could forego sentinel lymph node biopsy

In the study, no patients who received a low-risk DecisionDx-Melanoma test result, which predicts a less than 5%

risk of sentinel lymph node (SLN) positivity, had a positive SLNB. Additionally, the data showed that using DecisionDx-Melanoma to guide risk-aligned patient care could reduce the number of unnecessary SLNBs by 37% overall, 63% for T1a tumors and 50% for T1b tumors, specifically. In the study, DecisionDx-Melanoma achieved 100% sensitivity, demonstrating its potential to identify patients likely to experience SLN metastasis. This study involved patients with cutaneous melanoma (CM) tumors (T1-T2a) located in the head or neck region who had undergone SLNB (n=159). CM tumors on the head or neck tend to be more aggressive and pose unique challenges for SLNB surgery.

"These data reinforce those from our recently published DECIDE study,[1] showing that use of DecisionDx-Melanoma to inform decisions around the SLNB surgical procedure could reduce the number of unnecessary procedures performed, particularly in patients with a low risk of metastasis," said Matthew Goldberg, M.D., F.A.A.D., board-certified dermatologist and dermatopathologist, and medical director of Castle Biosciences. "Incorporating DecisionDx-Melanoma into clinical care plans when considering an SLNB can help identify patients who could forego the procedure."

Inflammatory Skin Disease Pipeline Test

Poster title: Survey results identifying clinician strategies for therapy selection for common inflammatory skin diseases

The poster shares results from a survey of 265 clinicians conducted during the 2022 Winter Clinical Dermatology Conference. Clinicians were asked various questions to determine how they choose a systemic therapy for their patients with moderate-to-severe atopic dermatitis (AD) or psoriasis (PsO) in the absence of a molecular test to help guide therapeutic selection, and how often their current approach leads to patients switching medications. The survey found that while reported efficacy was rated as the most important factor in guiding therapy selection for a patient, 62.3% of clinicians responded that, on average, two or more systemic therapies were needed to find one that was efficacious for their patients. More than 90% of clinicians surveyed indicated they would or would likely find a molecular test to guide therapy selection for AD or PsO beneficial.

While there are many effective treatments options available for those with moderate-to-severe AD or PsO, current clinical practice relies on a trial-and-error approach for therapy selection. To answer this unmet clinical need, Castle is developing a gene expression profile (GEP) test to predict response to systemic therapy in patients with moderate-to-severe AD, PsO and related inflammatory skin diseases. Personalized guidance for therapy selection and anticipated efficacy, based on each patient's molecular data, has the potential to improve patient health outcomes by enabling clinicians to better select a medication for their patients' specific skin disease.

Early development data for Castle's pipeline test for inflammatory skin diseases is expected in 2023, with an

expected launch by the end of 2025.

About DecisionDx®-Melanoma

DecisionDx-Melanoma is a gene expression profile risk stratification test. It is designed to inform two clinical questions in the management of cutaneous melanoma: a patient's individual risk of sentinel lymph node (SLN) positivity and a patient's personal risk of melanoma recurrence and/or metastasis. By integrating tumor biology with clinical and pathologic factors using a validated proprietary algorithm, DecisionDx-Melanoma is designed to provide a comprehensive and clinically actionable result to guide risk-aligned patient care. DecisionDx-Melanoma has been shown to be associated with improved patient survival and has been studied in more than 10,000 patient samples. DecisionDx-Melanoma's clinical value is supported by more than 40 peer-reviewed and published studies, providing confidence in disease management plans that incorporate the test's results. Through Dec. 31, 2022, DecisionDx-Melanoma has been ordered 120,287 times for patients diagnosed with cutaneous melanoma. More information about Castle's tests can be found at **www.CastleTestInfo.com**.

About Psoriasis, Atopic Dermatitis and Related Conditions

Inflammatory skin disease accounts for a significant number of patient visits to both primary care and dermatology clinics across the United States every year. Psoriasis and atopic dermatitis are among the most common inflammatory skin conditions, and patient quality of life is severely impacted by these chronic diseases. Fortunately, systemic medications developed over the past 15 years have demonstrated a significant improvement in patients' lives. In the United States alone, there are about 18 million patients diagnosed with psoriasis and atopic dermatitis, and approximately 450,000 patients annually are eligible for these systemic therapies. While there are now many effective treatments options available for those with moderate-to-severe inflammatory skin diseases, current clinical practice relies on a trial-and-error approach for therapy selection. To answer this unmet clinical need, Castle Biosciences is developing a gene expression profile test to predict response to systemic therapies for patients with moderate-to-severe psoriasis, atopic dermatitis and other related diseases.

About Castle Biosciences

Castle Biosciences (Nasdaq: CSTL) is a leading diagnostics company improving health through innovative tests that guide patient care. The Company aims to transform disease management by keeping people first: patients, clinicians, employees and investors.

Castle's current portfolio consists of tests for skin cancers, uveal melanoma, Barrett's esophagus and mental health conditions. Additionally, the Company has active research and development programs for tests in other diseases with high clinical need, including its test in development to predict systemic therapy response in patients with

moderate-to-severe psoriasis, atopic dermatitis and related conditions. To learn more, please visit **www.CastleBiosciences.com** and connect with us on **LinkedIn**, **Facebook**, **Twitter** and **Instagram**.

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: (i) the potential of DecisionDx-Melanoma test results to reduce the number of unnecessary SLNBs, particularly in patients with a low risk of metastasis, and identify patients likely to experience SLN metastasis and patients that can forego the SLNB procedure; (ii) the potential of p ersonalized guidance for therapy selection and anticipated efficacy, including our pipeline test for inflammatory skin diseases, to improve patient health outcomes by enabling clinicians to better select a medication for their patients' specific skin disease ; and (iii) our expectation that early development data for our pipeline test for inflammatory skin diseases will be available in 2023 and that the test will launch by the end of 2025. The words "can," "could," "expect," "potential" and similar expressions are intended to identify forward-looking statements, although not all forward-looking statements contain these identifying words. We may not actually achieve the plans, 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 our 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 this study and/or survey, including with respect to the discussion of DecisionDx-Melanoma and our pipeline test for inflammatory skin diseases in this press release; actual application of our tests may not provide the aforementioned benefits to patients; and the risks set forth under the heading "Risk Factors" in our Quarterly Report on Form 10-Q for the three months ended September 30, 2022, 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. Yamamoto M, Sickle-Santanello B, Beard T, et al. The 31-gene expression profile test informs sentinel lymph node biopsy decisions in patients with cutaneous melanoma: results of a prospective, multicenter study [published online ahead of print, 2023 Jan 16]. Curr Med Res Opin. 2023;1-7. doi:10.1080/03007995.2023.2165813

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Source: Castle Biosciences, Inc.