Empowering people, **informing** care decisions

AdvanceAD-Tx™

November 2025

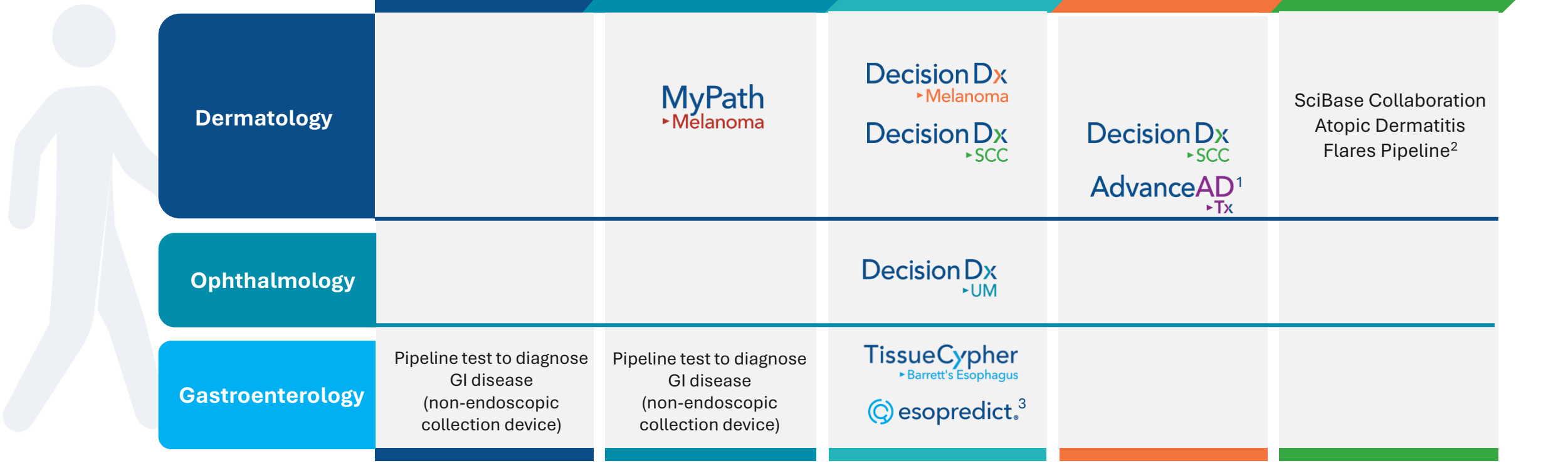
CASTLE BIOSCIENCES

Disclaimers

Forward-Looking Statements

This presentation 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: our positioning for continued growth and value creation; our estimated U.S. total addressable market for our commercially available tests; our ongoing studies generating data and their impact on driving adoption of our tests; study observations and interpretations of study data, including conclusions about the benefits and impact of our tests on treatment decisions and patient outcomes; our ability to advance penetration of our tests with clinicians and payers; our ability to carry out our commercial strategies; our ability to be net operating cash flow positive by the end of 2025; our future approach to capital allocation; our expected launch of our pipeline expansion by the end of 2025; the ability to combine spatialomics and DNA methylation for a multiomics approach to patient care; pipeline opportunities to expand screening and diagnostic support for patients with Barrett's esophagus (BE); test volume growth expectations; and the timing and achievement of program milestones. The words "anticipates," "can," "could," "estimates," "expects," "may," "potential," "target" 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: our estimates and assumptions underlying our estimated U.S. total addressable market for our commercially available tests; our assumptions or expectations regarding continued reimbursement for our products and subsequent coverage decisions; Novitas' local coverage determination signifying non-coverage by Medicare of our DecisionDx-SCC test; our estimated total addressable markets for our products and product candidates; the expenses, capital requirements and potential needs for additional financing, the anticipated cost, timing and success of our product candidates; our plans to research, develop and commercialize new tests; our ability to successfully integrate new businesses, assets, products or technologies acquired through acquisitions; the effects of macroeconomic events and conditions, including inflation and monetary supply shifts, tariffs and disruptions to trade, labor shortages, liquidity concerns at, and failures of, banks and other financial institutions or other disruptions in the banking system or financing markets and recession risks, supply chain disruptions, outbreaks of contagious diseases and geopolitical events (such as the ongoing Israel-Hamas War and Ukraine-Russia conflict), among others, on our business and our efforts to address its impact on our business; the possibility that subsequent study or trial results and findings may contradict earlier study or trial results and findings or may not support the results discussed in this presentation, including with respect to the diagnostic and prognostic tests discussed in this presentation; our planned installation of additional equipment and supporting technology infrastructures and implementation of certain process efficiencies may not enable us to increase the future scalability of our TissueCypher Test; the possibility that actual application of our tests may not provide the anticipated benefits to patients; the possibility that our newer gastroenterology and mental health franchises may not contribute to the achievement of our long-term financial targets as anticipated; and the risks set forth under the heading "Risk Factors" in our Annual Report on Form 10-K for the year ended December 31, 2024, and our Quarterly Report on Form 10-Q for the three months ended September 30, 2025, each 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.

Answering clinical questions to guide care along the patient journey



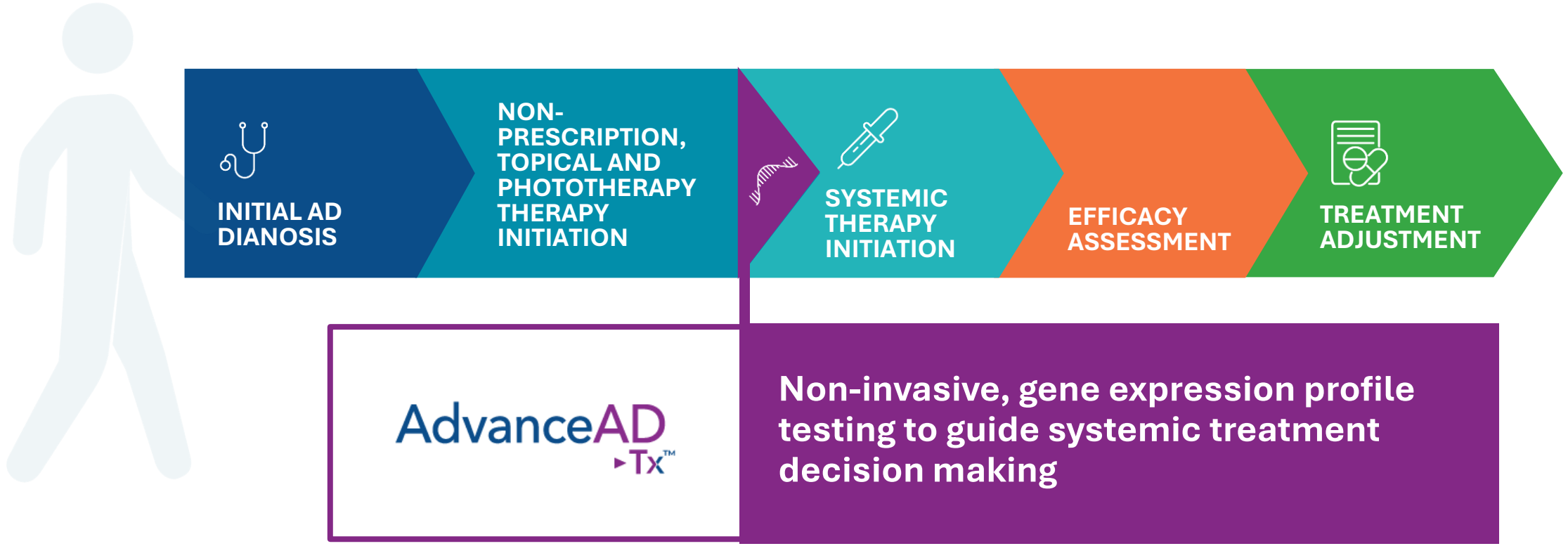
1. In November 2025, CSTL announced the launch of AdvanceAD-Tx, the Company's new test designed to guide systemic treatment decision making in patients ages 12+ with moderate-to-severe atopic dermatitis
2. Collaboration and license agreement with SciBase Holding AB ("SciBase") announced in June 2025
3. Acquisition of Capsulomics, Inc., d/b/a Previse announced in May 2025

Introducing AdvanceAD-Tx

Product Description	**A non-invasive gene expression profile test to guide systemic treatment decision making in patients with moderate-to-severe atopic dermatitis (AD)**
Test Mechanism	Sample is processed for RNA isolation and transcriptomic profiling, and a proprietary suite of neural networks evaluates 12 inflammatory and cutaneous biology pathways (487-genes) to classify patients into one of two results: JAKi Responder Profile or Th2 Molecular Profile.
Intended Use Population	Moderate-to-severe atopic dermatitis patients, ≥12 years of age. Clinical validation study included both systemic-naïve and previously treated patients.
Sample Collection	Non-invasive, lesional skin scrape (epidermal surface scaping). No biopsy required.
Turn-Around-Time	7 – 10 business days from receipt of sample.
Test Results	**JAK Inhibitor Responder Profile:** Gene expression profile is associated with a significantly higher clinical benefit from JAK inhibitor treatment. **Th2-Molecular Profile:** Gene expression profile is associated with similar clinical benefit regardless of treatment with a Th2-targeted or JAKi therapy.
Clinical Benefit	**JAK Inhibitor Responder Profile:** In clinical validation study, patients with this profile who were treated with a JAK inhibitor were significantly more likely to achieve EASI-90 and vIGA-AD 0 (clear), experienced greater reductions in itch and flares, and reached these endpoints faster than those treated with a Th2-targeted therapy **Th2 Molecular Profile:** In clinical validation, patients with this profile show no statistical difference in the likelihood of achieving optimal response when treated with either a JAKi or a Th2-targeted therapy by 3 months.

JAKi=Janus kinase inhibitors, Th2= T helper type 2; Eczema area and severity index improvement of 90% =EASI90; Validated Investigator Global Assessment scale for Atopic Dermatitis=vIGA-AD

Advancing the patient care journey in AD



The burden of AD

AD affects as many as **1 in 6 children** and **1 in 14 adults**[1]

~95% of patients report that the **major symptom** is unbearable itch[2,3]

~94% of AD households reported financial impact, with 24.5% reporting the impact as "severe" or "devastating"[4]

AD can affect **attendance** and **performance** at work, **sick leave**, and **job choice**[5]

Reported sleep disturbance as high as **90%** in children[6] and **80%** in adults[7]

People with atopic dermatitis are up to **44%** more likely to exhibit suicidal ideation, and **36%** more likely to attempt suicide[5]

Patients with AD experience an average of 3–10 flares per year, each lasting ~10–15 days[8]

AD **limits lifestyles**[9], **impacts relationships** and **physical activity**[9,10,11]

AD **negatively impacts** an individual's **quality of life** as well as that of the wider family[9]

1. Atopic dermatitis in the pediatric population. Silverberg, Jonathan I. et al. Annals of Allergy, Asthma & Immunology, Volume 126, Issue 4, 417 - 428.e2; Hadi HA, Tarmizi AI, Khalid KA, Gajdács M, Aslam A, Jamshed S. The Epidemiology and Global Burden of Atopic Dermatitis: A Narrative Review. Life (Basel). 2021 Sep 9;11(9):936. doi: 10.3390/life11090936. PMID: 34575085; PMCID: PMC8470589. 2. Feldman S, et al. *Am Health Drug Benefits*. 2019. 3.National Eczema Association. https://nationaleczema.org/blog/science-of-itch/. 4. Raj C, et al. Skin Health and Disease. 2023. 5. Association Between Atopic Dermatitis and Suicidality: A Systematic Review and Meta analysis by Sandhu JK, Wu KK, Bui TL, et al., published in *JAMA Dermatology* (2019;155(2):178-187) (online December 2018). 6. Sandhu JK, et al. *JAMA Dermatol*. 2019. 7. Fatima Bawany, Carrie A. Northcott, Lisa A. Beck, Wilfred R. Pigeon, Sleep Disturbances and Atopic Dermatitis: Relationships, Methods for Assessment, and Therapies, The Journal of Allergy and Clinical Immunology: In Practice, Volume 9, Issue 4, 2021, Pages 1488-1500, ISSN 2213-2198, https://doi.org/10.1016/j.jaip.2020.12.007. (https://www.sciencedirect.com/science/article/pii/S2213219820313398). 8. Gray C. et al., 2024 – Targeted Literature Review (Sanofi); Wollenberg A. et al., 2022, *Curr Opin Allergy Clin Immunol*; Nielsen M-L et al., 2025, *JAMA Dermatology*; Simpson E. et al., 2018, *Dermatitis*; Silverberg JI et al., 2016, *Ann Allergy Asthma Immunol*. 9. Caffrey. *AMJC*. 2017. 10. Silverberg, et al. *J Invest Dermatol*. 2016. 11. Tsung-Hsun Y. et al. *Int J Environ Res Public Health*. 2022.

Match treatments to each patient's immune profile using advanced testing methods

With the potential to eliminate trial and error

Suboptimal initial systemic therapy leads to:

- **Delayed disease control**
- **Patient dissatisfaction**
- **Increased healthcare utilization**

Opportunity

Stratify patients upfront based on immune signature to improve treatment success.

This personalized approach is designed to identify the specific immune pathways that need treatment in each patient.

AdvanceAD-Tx

Intended Use Population

Based on a one-year prevalence, it is estimated that there are approximately 13.2 million patients ages 12 and older in the United States with moderate-to-severe AD

Launch Details

AdvanceAD-Tx is being made commercially available through a measured, limited access launch (via existing commercial team) beginning November 2025, with phased, expanded availability anticipated through 2026

Total Addressable Market (TAM)

Target population represents an estimated ~$33 billion U.S. opportunity

Reimbursement Strategy

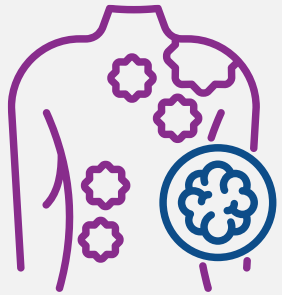
Pursuing multiple reimbursement pathways

Atopic Dermatitis in America Study: A Cross-Sectional Study Examining the Prevalence and Disease Burden of Atopic Dermatitis in the US Adult Population. DOI:https://doi.org/10.1016/j.jid.2018.08.028
Patient burden and quality of life in atopic dermatitis in US adults: A population-based cross-sectional study. DOI:https://doi.org/10.1016/j.jid.2018.08.028

IDENTITY Study:
Development and validation of a precision medicine test for atopic dermatitis

AdvanceAD-Tx helps identify systemic treatment response in patients with moderate-to-severe atopic dermatitis

Moderate-to-severe AD patient ≥12 years



AdvanceAD-Tx

- Quantifies expression of 487 genes from 12 inflammatory pathways associated with AD
- Applies a validated neural network algorithm
- Designed to guide systemic treatment decision making for patients

JAK Inhibitor Responder Profile
Gene expression profile is associated with a significantly higher clinical benefit from JAK inhibitor treatment

Th2 Molecular Profile
Gene expression profile is associated with similar clinical benefit regardless of treatment with a Th2-targeted or JAKi therapy

AdvanceAD-Tx results are intended to aid, not replace, clinical judgment. All treatment decisions should be made by the clinician in the context of the patient's overall clinical picture.

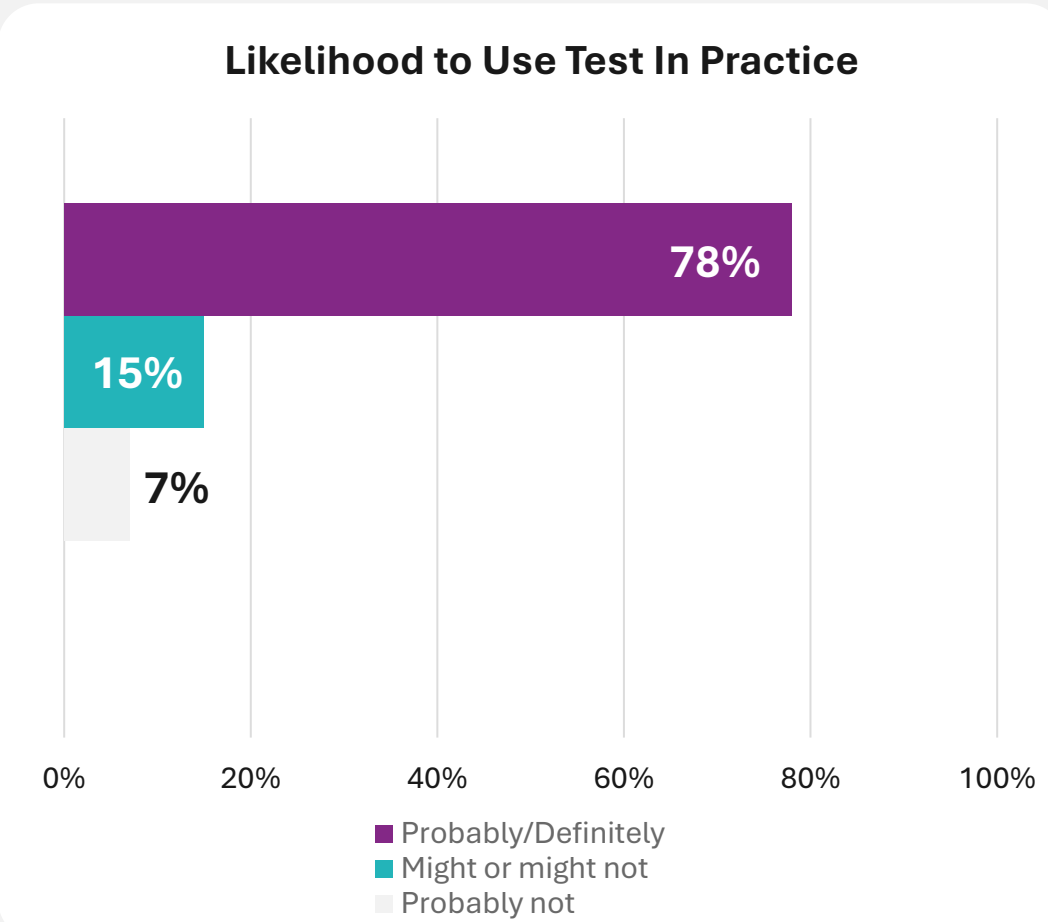
Data from the IDENTITY Study

Patients with JAKi Responder Profile who are treated with a JAK inhibitor therapy, compared to those treated with a Th2-targeted therapy achieve the following by 3 months:

- Achieved a higher rate of EASI-90 (45.5% vs 8.3%, p=0.021)
- More likely to achieve a validated investigator global assessment score of clear (vIGA-AD 0, 36.4% vs 0%, p=0.006)
- More likely to remain flare-free during treatment (54.5% vs. 16.7%, p=0.041)
- More likely to report “no itch” by three months (45.5% vs. 8.3%, p=0.021)
- Reached EASI-90 3.8 times faster (p=0.049)

Adapted from Silverberg J, et al. The 487-gene expression profile test guides systemic therapy selection to improve outcomes for patients with atopic dermatitis: Results from a prospective, multi-center trial. Fall Clinical Dermatology Conference. 10.3.2025
Eczema area and severity index improvement of 90% =EASI90.

Market research showed most respondents “definitely” or “probably” would use AdvanceAD-Tx, provided coverage is assured



- Among the overall sample, **approximately 80% of HCPs** stated that they would “definitely” or “probably” use the test

- Reasons that surfaced among respondents more likely to use the test centered on…
  - ***Improved patient outcomes***
  - **Streamline decision-making** and reducing delays
  - Aligning with the future of medicine – **precision medicine**

“I am in the category of ‘definitely would’… the idea of having a tool to streamline the process better and get better outcomes is very appealing. I would consider it for all of my AD patients if I could get it covered.” (DERM,MD)

Castle Biosciences primary qualitative market research with Dermatologists and NP/PAs, August 2025

DERMATOLOGY

AdvanceAD-Tx

A non-invasive molecular test that is designed to detect the underlying immune biology of atopic dermatitis (AD) that is driving an individual patient's AD and thus helps to guide systemic treatment decision making in patients with moderate-to-severe AD

Validated in Real-World Patients

- The AdvanceAD-Tx test has been clinically validated in patients 12 years and older with moderate-to-severe AD. The clinical validation study included both systemic treatment naïve patients and those who were on a systemic treatment but considering a switch in therapy.
- The test can be ordered at any point in the patient's treatment journey and provides valuable molecular insight to help guide therapy-class selection. Ordering the test early may help reduce uncertainty, minimize trial-and-error, and support more timely disease control.

~13.2m

patient population of moderate-to-severe AD patients 12+ year of age, based on one-year prevalance[1]

~27%

of patients who started on an advanced biologic or JAKi switched to another advanced systemic therapy[2]

~$33 billion Estimated U.S. TAM[3]

1. Atopic Dermatitis in America Study: A Cross-Sectional Study Examining the Prevalence and Disease Burden of Atopic Dermatitis in the US Adult Population. DOI:https://doi.org/10.1016/j.jid.2018.08.028. Patient burden and quality of life in atopic dermatitis in US adults: A population-based cross-sectional study. DOI:https://doi.org/10.1016/j.jid.2018.08.028
2. https://pmc.ncbi.nlm.nih.gov/articles/PMC11904833/pdf/ActaDV-105-41504.pdf;
3. U.S. TAM = Total addressable market based on estimated patient population assuming average reimbursement rate among all payors.

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