



AltheaDx Acquisition  
& Business Update

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April 4, 2022



# 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 are typically identified by the words “anticipates,” “believes,” “estimates,” “expects,” “intends,” “may,” “plans,” “projects,” “will,” “would” and similar expressions, although not all forward-looking statements contain these identifying words. Forward-looking statements in this presentation include, but are not limited to, statements concerning: the anticipated consummation of the acquisition of AltheaDx and the expected timing and actual closing of the transactions contemplated thereby, and the expected benefits resulting therefrom; our objectives, expectations (financial or otherwise) and intentions, future financial results and growth potential, including our expected estimated U.S. TAM for IDgenetix following our anticipated acquisition of AltheaDx; updates in our financial guidance for the 2022 fiscal year after giving effect to the anticipated acquisition of AltheaDx; our anticipated product portfolio and pipeline opportunities, including our ability to integrate IDgenetix into our existing portfolio of commercial offerings; the ability of the AltheaDx and Castle teams to successfully collaborate and the ability of IDgenetix to complement our portfolio of personalized testing solutions and enable our growth with advancement into pharmacogenomics and mental health; the ability of IDgenetix to accelerate our impact on patients with mental health conditions, enable us to offer incremental value to patients and clinicians over standard of care and potentially develop a mental health franchise; our belief that both drug-gene and drug-drug interactions may impact the effectiveness of individual therapies; and our belief that IDgenetix provides important genetic information that has the potential to help improve patients’ chances of response and/or remission by identifying appropriate medications more efficiently than the standard of care trial. 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, risks related to our ability to complete the acquisition of AltheaDx on the proposed terms and schedule, including risks and uncertainties related to the satisfaction of closing conditions, which may result in the conditions to closing not being satisfied and the transaction being delayed or not being ultimately consummated; risks associated with business combination transactions, such as the risk that acquired businesses will not be integrated successfully or that such integration may be more difficult, time-consuming or costly than expected; the calculations of, and factors that may impact the calculations of, the expected estimated U.S. TAM for IDgenetix, which may prove to be inaccurate; expanded Medicare reimbursement coverage for IDgenetix may never be granted, which could reduce our expected estimated TAM for IDgenetix; our assumptions underlying the anticipated contributions from the AltheaDx acquisition to our 2022 financial guidance, which could be inaccurate; risks related to future opportunities and plans for our company following our anticipated acquisition of AltheaDx, including uncertainty of our expected financial performance and results of our company following completion of the proposed acquisition; disruption from the proposed acquisition, making it more difficult to conduct business as usual or maintain relationships with customers, employees or suppliers; changes in market conditions and the introduction of competitive technologies, as well as competition from other commercial-stage diagnostics companies with PGx offerings for the treatment of depression, anxiety or other mental health conditions; the impact of unanticipated regulatory obligations and oversight; our expectations regarding reimbursement for IDgenetix or tests currently in our commercial portfolio; the effects of the COVID-19 pandemic on our business and our efforts to address its impact on our business; IDgenetix’s ability to provide the aforementioned benefits to 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, 2021, 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.



## Castle Remains Focused On Transforming Disease Management

Strategic principles that create value for customers, patients and stockholders



Address areas  
with unmet  
clinical need



Leverage advanced  
technologies for  
innovative tests



Provide robust data to  
support the clinical  
value of our tests



Accelerate test  
adoption through  
commercial excellence



## IDgenetix Fits Within Our Focus On Transforming Disease Management

Leveraging Castle's history of commercial success to accelerate adoption



Address areas  
with unmet  
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Leverage advanced  
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Provide robust data to  
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**Accelerate test  
adoption through  
commercial excellence**



# Potential Acquisition Expected to Provide Strength to Castle's Portfolio of Tests and Long-Term Potential in Other Areas of Mental Health Therapeutic Response

## Opportunity

- IDgenetix test represents an estimated ~\$5B U.S. Total Addressable Market (TAM) for mental health
- IDgenetix reimbursed by Medicare for depression since 2020
- IDgenetix randomized controlled clinical-use trial demonstrated clinical utility over standard of care, when physicians used the test prior to prescribing a medication<sup>1</sup>

## Strategic Fit

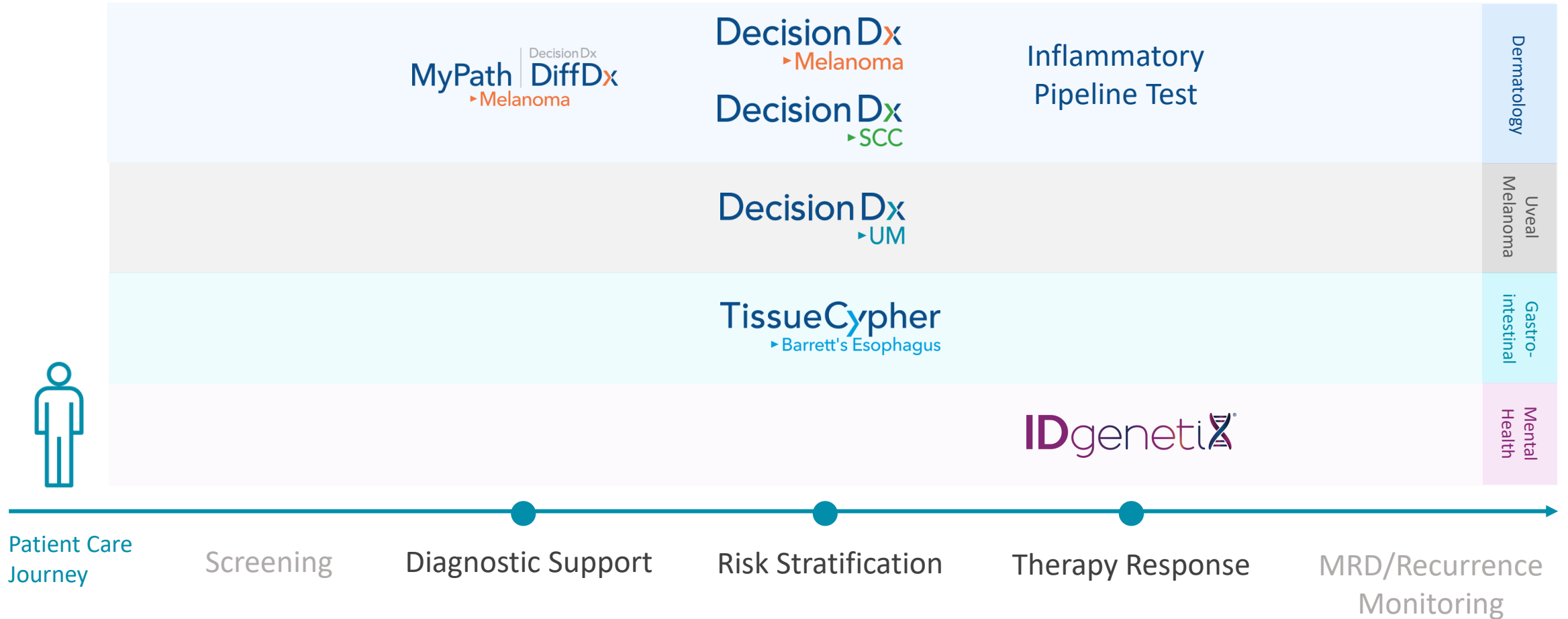
- An area where we can leverage our commercial success
- Potential to create a suite of tests in a single call point
- Ability to answer clinical questions/impact patient care
- Early reimbursement wins

## Value Rationale

- Expands expertise into areas of mental health and treatment response through pharmacogenomic (PGx) testing
- Provides ability to build pipeline in an adjacent market (aligns with inflammatory skin disease pipeline test)
- Acquisition expected to contribute to near- and long-term revenue growth

# IDgenetix Aligns with our Therapy Response Touchpoint Along the Patient Care Continuum

Answering clinical questions to guide care along the patient journey



# Including IDgenetix, Anticipate an Estimated ~\$8B for Commercially Available U.S. Total Addressable Market<sup>1</sup>

Dermatology			Gastroenterology	Mental Health
Cutaneous melanoma/ risk of metastasis	Cutaneous squamous cell carcinoma/ risk of metastasis	Suspicious pigmented lesions/melanoma status	Barrett's esophagus/ risk of progression to esophageal cancer	Mental Health therapy response
~130K Patients classified as Stage I, II or III <sup>2</sup>	~200K Patients w/ high-risk features <sup>2</sup>	~300K Patients w/ indeterminant biopsy <sup>2</sup>	~384K Patients receiving upper GI endoscopies/year who meet the intended use criteria for TissueCypher <sup>3</sup>	Based on indicated use of IDgenetix for patients diagnosed with depression, anxiety and other mental health conditions
~\$540M	~\$820M	~\$600M	~\$1B	~\$5B

**Tests in pipeline add an additional estimated ~\$3.6B to our U.S. TAM**  
 (\$1.9B for inflammatory pipeline test and ~1.7B for additional dermatology pipeline tests)

<sup>1</sup>U.S. TAM = Total addressable market based on estimated patient population assuming average reimbursement rate among all payors.

<sup>2</sup> Annual U.S. incidence for Stage I, II or III melanoma estimated at 130,000; annual U.S. incidence for squamous cell carcinoma estimated at 1,000,000 with addressable market limited to carcinomas with one or more high risk features; annual U.S. incidence for suspicious pigmented lesion biopsies estimated at 2,000,000 with addressable market limited to the 15% with an indeterminant biopsy.

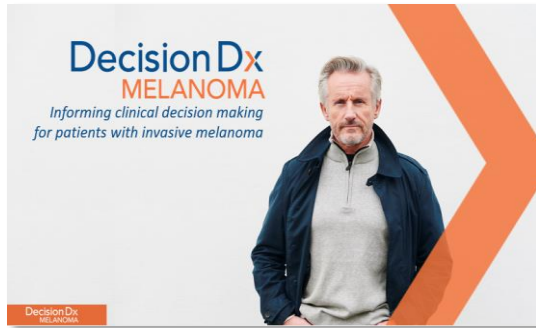
<sup>3</sup>384,000 upper GI endoscopies/year with confirmed dx of BE (ND, IND, LGD) x \$2,513 = U.S. only TAM of ~\$1 billion



# Pillars Of Our Growth Plan

Consistent execution furthers our leading position in dermatology and in the Dx space

## Strong Core Derm Business



- Continuing provider education
- Optimizing commercial team
- Evolving our go-to-market strategy (EMA, VA)
- NCI/SEER collaboration



## Pipeline Initiatives



- Ability to answer clinical questions/impact patient care
- Utilizing our areas of expertise (genomics, spatialomics, AI) to develop innovative tests
- Focusing on complementary/adjacent disease states

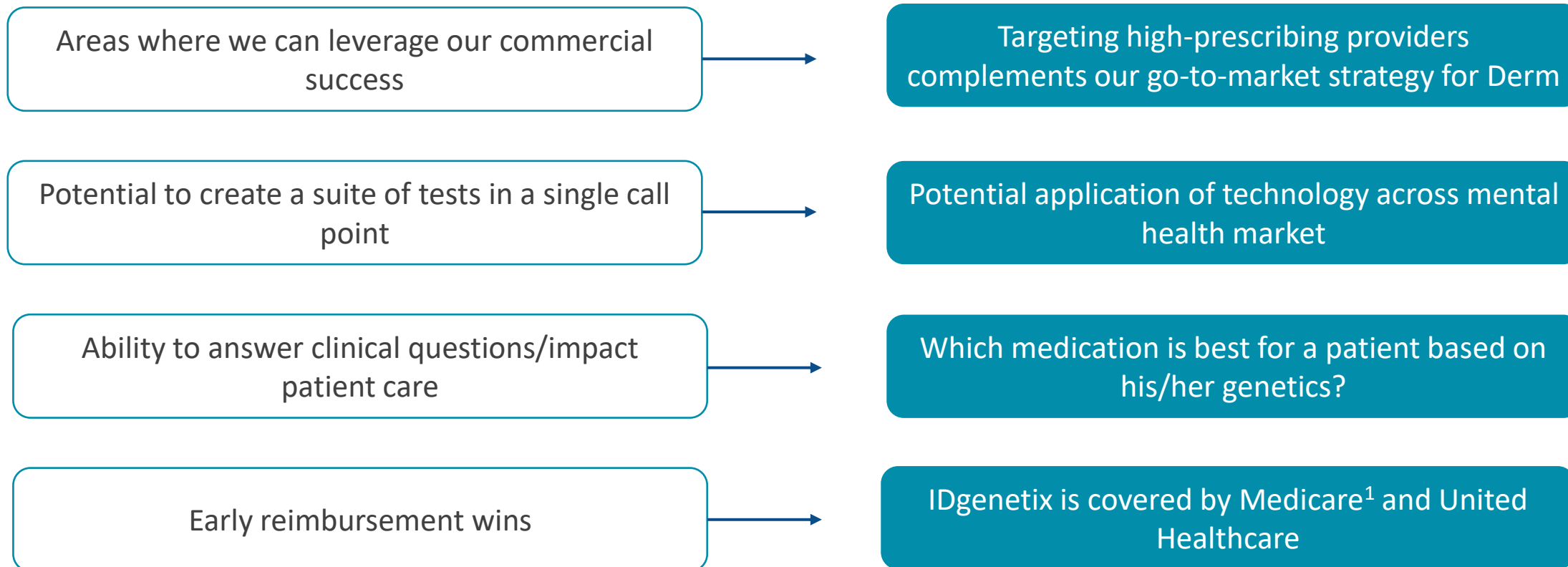


## Strategic Opportunities



- **Areas where we can leverage our commercial success**
- **Potential to create a suite of tests in a single call point**
- **Ability to answer clinical questions/impact patient care**
- **Early reimbursement wins**

## Anticipated Acquisition Aligns With Castle's M&A Strategy



*Our capital allocation priorities include strategic acquisitions with potential for mid- to long-term value creation and revenue and earnings growth*

9 <sup>1</sup>The Medicare reimbursement rate is currently ~\$1,500 for IDgenetix multi-gene testing for depression.



## About AltheaDx

Finding effective medications to treat mental health disorders

# ALTHEA<sup>Dx</sup>

A commercial-stage molecular diagnostics company specializing in the field of pharmacogenomics (PGx). IDgenetix<sup>®</sup> is AltheaDx's PGx product test for depression, anxiety and other mental health conditions.

- IDgenetix<sup>®</sup>, a PGx test for depression, anxiety and other mental health conditions
- CAP-accredited, CLIA-certified laboratory, authorized to offer IDgenetix in all 50 states
- Approved by the New York State Department of Health



IDgenetix<sup>®</sup>



## Transaction and Transition Snapshot

\$65 million in cash  
and stock due at  
closing<sup>1</sup>

Up to an additional  
\$75 million payable in  
cash and stock, based on  
the achievement of  
certain milestones<sup>1</sup>

Expected close during  
Q2 2022

Expect AltheaDx's  
staff to join Castle  
team, including  
commercial team

Existing commercial  
team of ~20 outside  
sales territories will  
report to Castle's chief  
commercial officer

## Full-Year 2022 Guidance

	As of February 28, 2022 <sup>1</sup>	Key Drivers	As of April 4, 2022 <sup>2</sup> Incremental attributed to AltheaDx
<b>Revenue</b>	\$115 - \$120 million		<b>~\$1-3 million</b>
<b>Cost of Sales</b> (exclusive of amortization of acquired intangible assets)	65%-75% growth	Scaling of Pittsburgh lab; preparation for volume ramp for TissueCypher, DecisionDx-SCC and DiffDx-Melanoma ahead of reimbursement	<b>~\$2-3 million</b>
<b>R&amp;D Expense</b>	50%-60% growth	Continued acceleration in R&D to support our dermatology, GI and pipeline tests, including increase in clinical research and additional headcount	<b>~\$1-2 million</b>
<b>SG&amp;A Expense</b>	30%-35% growth	Addition of gastroenterology team and continued build in dermatology	<b>~\$9-10 million</b>
<b>Stock Based Comp</b>	\$35-40 million	Primarily due to increase in headcount to support growth, with pace of additional employees increasing in recent years and 2022	<b>~\$3-4 million</b>

<sup>1</sup>Guidance given on February 28, 2022. Percentage increases compared to the year ended 12/31/21; Cost of sales, R&D and SG&A expense growth includes stock-based comp.

<sup>2</sup>Based on estimates and assumptions as of the date of this presentation and subject to change following completion of AltheaDx acquisition.

## Anticipated Acquisition Aligns With Castle's Capital Allocation Priorities



Deploy capital to effectively create meaningful stockholder value



Focus on strategic acquisitions with potential for mid- to long-term value creation and revenue and earnings growth



Further positions Castle as a leader in advanced diagnostics

## Depression/Major Depressive Disorder Is A Significant Burden

The rise in psychiatric conditions is one of many factors driving the potential need in PGx testing



**1 in 5 adults** in the U.S. experienced mental illness **in 2019**, compared to...



**1 in 10 adults in 2018**

New physicians entering the field may drive greater adoption and uptake in the future



**~15% of active mental health providers** ordered at least one PGx test to guide psychotropic medication prescriptions between 2017-2018...



**...while ~90% of medical students** believe genetic testing should be utilized if a genetic variant could help predict medication response or side effect risk

# IDgenetix Is Designed to Help Patients Diagnosed With Depression Get On Effective Prescription Drugs Faster

## The problem...

**47%** of patients diagnosed with depression *experience adverse reactions to their prescribed medications*<sup>1</sup>

**60%** of patients diagnosed with depression *do not show improvement with first-line therapies*<sup>2</sup>

**70-89%** of patients diagnosed with depression *do not achieve remission using current standard of care*<sup>3</sup>

A *higher number of treatment steps* is associated with *lower remission and higher relapse rates*<sup>3</sup>

## The solution...

IDgenetiX<sup>®</sup>

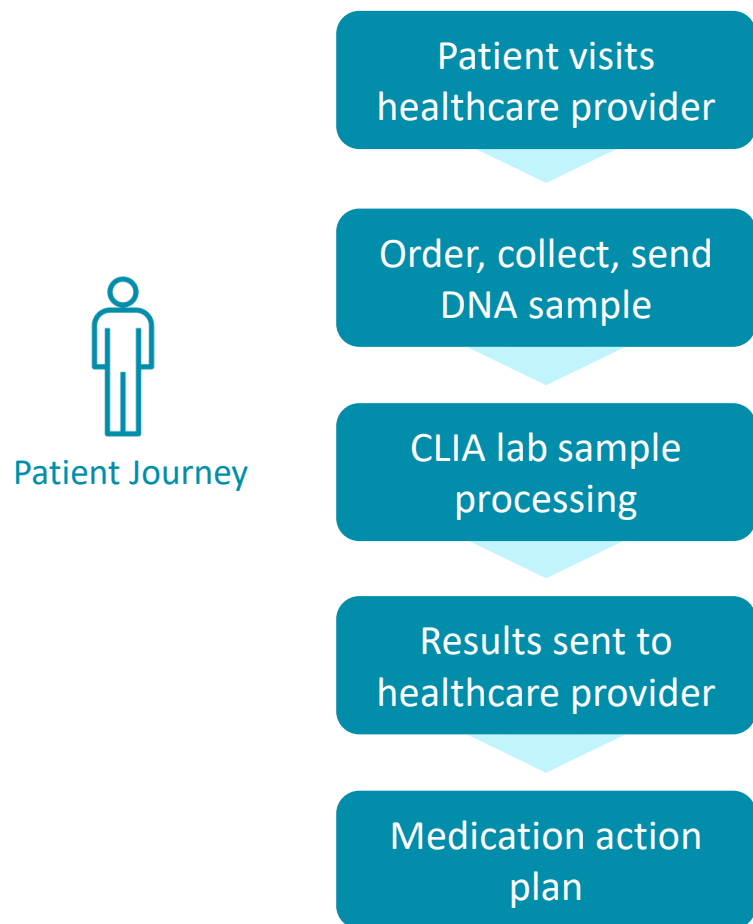
<sup>1</sup>Braund TA, et al., *Transitional Psychiatry* (2021)

<sup>2</sup><https://www.webmd.com/depression/fears-and-facts-about-antidepressants#:~:text=Four%20out%20of%2010%20people,one%20that%20works%20for%20them>, accessed March 30, 2022;

<sup>3</sup>Rush AJ, et al., *Am J Psychiatry* 163:11 (2006)

# Leveraging Pharmacogenomics (PGx) to Transform Patient Care In Mental Health

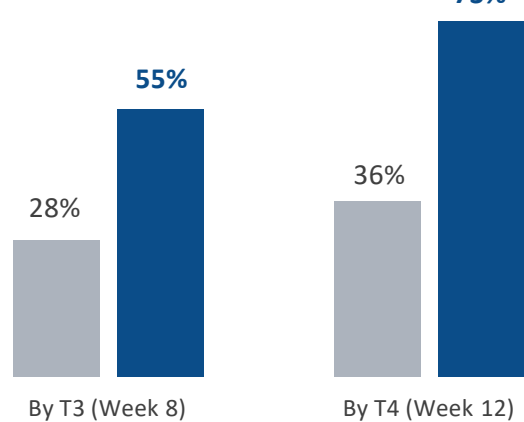
PGx testing may help patients get on effective prescription drugs faster



- Through a simple cheek swab to collect patient DNA, the IDgenetix test potentially enables physicians to achieve ***faster remission*** for patients
- Replacing standard-of-care trial-and-error prescription practices in mental health with a scientifically-backed genetic test has the potential to:
  - Optimize clinical outcomes
  - Reduce adverse events
  - Yield cost savings in the healthcare system

# Enhanced Therapeutic Efficacy vs. Standard of Care

## Response Rate ≥ 50% Reduction from Baseline



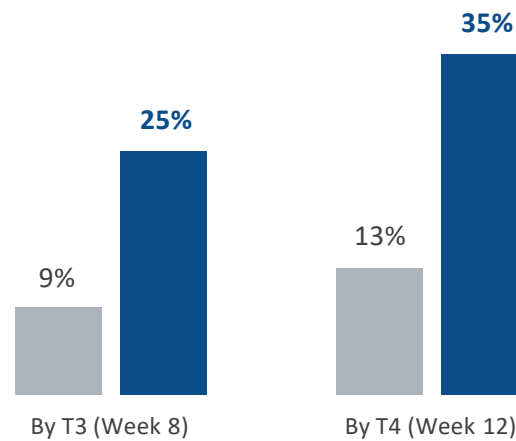
■ Control  
■ IDgenetix

p-value

0.01

0.001

## Remission Rate Back to Normal



p-value

0.05

0.02

## Clinical Trial Design

- Randomized Controlled Trial (RCT)
- Peer-reviewed and published in the *Journal of Psychiatric Research*
- 685 participants, Depression *and* Anxiety
- Double-blinded
- Treated by a broader group of medical professionals, beyond psychiatrists
- 20 independent clinical sites
- 4, 8 and 12-week efficacy using HAM-A scale



# IDgenetix Testing Process Consists of Three Important Steps

## 1 Drug Metabolism Genotyping

### PROCESS

Analyzes patient-specific genetic variants that influence the function of drug metabolizing enzymes

### IMPORTANCE

Influences how much of a drug is active in the body to produce therapeutic or toxic effects

Drug-Gene Interactions

## 2 Drug Response Genotyping

### PROCESS

Analyzes patient-specific genetic variants involved in the way medications work at the biologic site of action

### IMPORTANCE

Influences the likelihood of a therapeutic or adverse drug response

## 3 Algorithmic Screening

### PROCESS

Screens for metabolic interactions caused by concomitant prescription, OTC and herbal medications that may significantly alter the metabolism of approved medications

### IMPORTANCE

Identifies CYP450-mediated interactions that can alter which medications are optimal for each patient

Drug-Drug Interactions

*IDgenetix testing is designed to provide tailored treatment recommendations for each patient by utilizing a bioinformatic algorithm to integrate patient-specific health information with comprehensive genetic results*

## GI/TissueCypher Integration Update

Fueling mid- and long-term growth with TissueCypher® platform and GI franchise

- GI commercial team covering ~14 outside territories hired, trained and in the field in January 2022, with commensurate GI-focused medical science liaisons and internal sales associates
- Year-to-date 2022, two abstracts for GI conferences (podium presentations at ESGE Days 2022 and DDW 2022) and one peer-reviewed publication accepted<sup>1</sup>
- Leveraging spatialomics expertise to identify pipeline opportunities in GI and dermatology
- Lab floorplan and workflow reconfigurations have increased efficiencies with more progress expected throughout 2022
- Advanced Diagnostic Laboratory Test (ADLT) approval, effective March 24, 2022
  - Rate for initial period of \$2,350 (April 1, 2022-Dec. 31, 2022), set by PAMA thereafter
- Planned capex investments in Pittsburgh (lab space and headcount) expected to allow for further enhancements to automation and significant increases in throughput; these expansion efforts are expected to provide support for future tests using the spatialomics platform as well as processing DecisionDx-SCC and other of Castle's gene expression profile tests



# Expected Addition of AltheaDx Further Diversifies Castle's Portfolio of Innovative Tests



## Guiding Patient Care

- Castle is committing to improving health through innovative tests that guide patient care
- IDgenetix guides physician treatment to potentially eliminate ineffective treatment options for each patient
- May help patients get on effective prescription drugs faster



## Strong Strategic Fit

- Can leverage our commercial success
- Potential to create a suite of tests in a single call point
- Ability to answer clinical questions/ impact patient care
- Early reimbursement wins



## Value Proposition

- Expands expertise into area of pharmacogenomics and mental health
- Provides ability to build pipeline in an adjacent market (therapy response)
- Acquisition expected to contribute to near- and long-term revenue growth

# Castle is Committed to Addressing Patients' Unmet Clinical Need Through Innovative Testing

 **Dermatology<sup>1</sup>**

Decision Dx  
▶ Melanoma

Decision Dx  
▶ SCC

MyPath | Decision Dx  
DiffDx  
▶ Melanoma

 **Uveal Melanoma<sup>2</sup>**

Decision Dx  
▶ UM

 **Gastroenterology<sup>3</sup>**

TissueCypher  
▶ Barrett's Esophagus

 **Mental Health**

IDgenetiX

*Portfolio of innovative tests designed to guide patient care*



**C/STLE**  
BIOSCIENCES

Thank you

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