

INVESTOR CONFERENCE

SEPTEMBER 2023



CardioDiagnostics

Revolutionizing Cardiovascular Medicine
With Epigenetics and AI



Forward Looking Statements

Certain statements and information included in this presentation constitute "forward-looking statements" within the meaning of the Private Securities Litigation Act of 1995. When used in this presentation, the words or phrases “will”, "will likely result," "expected to," "will continue," "anticipated," "estimate," "projected," "intend," “goal,” or similar expressions are intended to identify "forward-looking statements" within the meaning of the Private Securities Litigation Reform Act of 1995. Such statements are subject to certain risks, known and unknown, and uncertainties, many of which are beyond the control of the Company. Such uncertainties and risks include, but are not limited to, our ability to successfully execute our growth strategy, changes in laws or regulations, economic conditions, dependence on management, dilution to stockholders, lack of capital, the effects of rapid growth upon the Company and the ability of management to effectively respond to the growth and demand for products and services of the Company, newly developing technologies, the Company’s ability to compete, regulatory matters, protection of technology, the effects of competition and the ability of the Company to obtain future financing. An extensive list of factors that can affect future results are discussed in the Current Report on Form 10-K for the period ended December 31, 2022 and 10-Q for the period ended March 31, 2023 under the heading “Risk Factors” in Part I, Item IA thereof, and other documents filed from time to time with the Securities and Exchange Commission. Such factors could materially adversely affect the Company's financial performance and could cause the Company's actual results for future periods to differ materially from any opinions or statements expressed within this presentation.

Key Investment Highlights

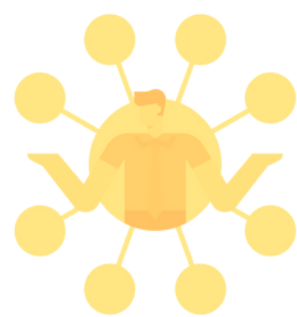
- NASDAQ listed: CDIO - market cap \$6 million as of 9/6/2023
- Cardio Diagnostics is an artificial intelligence-powered precision cardiovascular medicine company that makes cardiovascular disease prevention and early detection more accessible, personalized and precise
- Launched multiple products leveraging proprietary AI-Driven Integrated Genetic–Epigenetic Engine™:
 - **Epi+Gen CHD™**: only epigenetics-based test in the world for coronary heart disease risk assessment (**\$51 billion US TAM**)
 - **PrecisionCHD™**: only epigenetics-based test in the world for coronary heart disease detection (**\$134 billion US TAM**)
 - **Actionable Clinical Intelligence™**: a one-of-a-kind platform that offers new epigenetic and genetic insights to clinicians prescribing the Epi+Gen CHD™ and PrecisionCHD™ tests
 - **CardioInnovate360**: research-use-only (RUO) solution to support the discovery, development and validation of novel biopharmaceuticals for the assessment and management of cardiovascular diseases
- Cardio Diagnostics' products are:
 - More sensitive compared to current lipid-based clinical tests and stress ECG
 - Non-invasive clinical tests that can be completed remotely or in provider settings
 - Clear value propositions to scale across multiple channels including telemedicine, providers, payers, employers, pharma and life insurance
- Additional clinical tests for stroke, congestive heart failure & diabetes in development that together address a \$340B US Total Addressable Market ⁽¹⁾
- A highly experienced commercial and clinical team

⁽¹⁾ Source: Cardio Diagnostics estimate for US markets based on 2020 US Census data

Cardio Diagnostics' Mission is to Revolutionize Cardiovascular Medicine with Epigenetics and AI

Our Vision:

Precision Cardiovascular Medicine, driven by epigenetics and artificial intelligence, will transform the delivery of targeted interventions, enhance patient outcomes, and reduce costs, ultimately alleviating the global burden of heart disease.



**Risk
Assessment**



**Risk
Management**



**Disease
Screening**



**Early
Diagnosis**



**Medical Management
& Lifestyle
Modifications**



**Monitor
Effectiveness**



**Ongoing
Evaluation**



Cardio Diagnostics is Pioneering a New Era in Precision Cardiovascular Medicine Driven by Innovation, Diversification, Scale and Experience



INNOVATION

TECHNOLOGY

- Only precision molecular diagnostics technology for cardiovascular disease at the intersection of epigenetics, genetics and AI.
- AI-driven integrated Genetic-Epigenetic Engine™, a proprietary platform to rapidly design, develop, and launch clinical tests.

INTELLECTUAL PROPERTY

- Diverse and robust intellectual property portfolio.
- Consists of granted and pending patents, trade secrets and copyrights.

DIVERSIFICATION

PRODUCTS

- Multiple launched and in development synergistic clinical and non-clinical products addressing various cardiovascular diseases.
- Backed by robust clinical, analytical and economic studies that appeal to various healthcare stakeholders.

MARKETS

- Robust value propositions for key healthcare stakeholders, including providers, provider organizations, payers, employers, life insurance and pharma.
- Customized offering to meet the needs of different market segments.

Cardio Diagnostics is Pioneering a New Era in Precision Cardiovascular Medicine Driven by Innovation, Diversification, Scale and Experience



SCALE

OPERATIONS

- Highly scalable and efficient testing and reporting process.
- Favorable economies of scale to lower COGS and improve margin.

REVENUE

- >\$300B total addressable market across launched and in-development products.
- High potential for recurring revenue.

EXPERIENCE

CLINICAL

- Has profound understanding of clinical needs, challenges and opportunities.
- Deep expertise in designing, executing and publishing studies to expand evidence base, increase credibility and gain clinical and commercial acceptance.

BUSINESS

- Have successfully built and launched multiple healthcare products/services across private and public companies.
- Experience expanding into new markets and targeting new customers.

Cardiovascular Disease is the Leading Cause of Death Globally Despite Being Largely Preventable

#1

Cardiovascular disease (CVD) is the leading cause of death globally, accounting for nearly 19 million deaths per year, or about 32% of all global deaths ⁽¹⁾

\$47
TRILLION
LOSS

Globally, cardiovascular disease is expected to result in a cumulative output loss of \$47 trillion from 2011 to 2030 due to medical costs and productivity losses, representing 75% of the global GDP in 2010 ⁽²⁾ ⁽³⁾

72%

Following a healthy lifestyle may prevent 72% of premature deaths related to heart disease ⁽³⁾

Cardiovascular Disease is a Burden for All Major Stakeholders



Employers

Employers can face increased healthcare costs due to heart disease, as employees with cardiovascular disease have medical costs that are twice as high as those without the condition ⁽¹⁾



Providers and Provider Organizations

Heart disease accounts for approximately 25% of emergency room visits related to chest pain, which can strain hospital resources, particularly in emergency departments ⁽²⁾



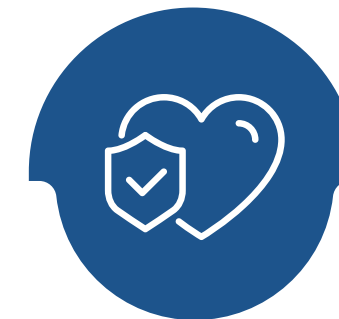
Payers

Heart disease is responsible for a substantial portion of healthcare expenditure. In 2015, around 14% of total U.S. healthcare expenditure was attributed to cardiovascular disease ⁽¹⁾



Patients

In the United States, heart disease is responsible for approximately 659,000 deaths annually, which equates to 1 in every 4 deaths ⁽³⁾



Life Insurers

As the number one killer, heart disease is a leading cause of life insurance payouts

Four Strategic Steps to Realize Our Vision



1 Build comprehensive evidence that matter to key healthcare stakeholders

- Rigorous clinical and analytic validation of biomarkers and Artificial Intelligence models
- Health economic studies to demonstrate substantial savings and ROI

2 Establish a robust product pipeline

- Leverage proprietary AI-Driven Integrated Genetic-Epigenetic Engine™ to complete the development and launch of new synergistic tests
- Diverse suite of tests to address major types of cardiovascular diseases across the care continuum

3 Take a strategic approach to commercialization

- Establish strong partnerships with key healthcare stakeholders to accelerate market entry and enhance overall business success
- Be present in diverse markets to expand customer base, reduce risks and capitalize on new opportunities to foster growth and resilience in the short and long-terms

4 Execute on meaningful initiatives to broaden adoption

- Foster strong relationships with payers to secure reimbursement towards driving sustained revenue growth and market penetration
- Consider going through the FDA pathway to continue to build trust among clinicians and patients
- Engage thought leaders to advocate for the clinical benefits, enhance credibility within the medical community, and foster widespread acceptance and utilization

Clinicians' Current Approach to Assessing Risk for and Detecting Cardiovascular Disease

Currently, risk for CVD is assessed using two common lipid-based clinical tests:

FRAMINGHAM RISK SCORE (FRS)

- Age
- Gender
- Systolic blood pressure
- Diabetes
- Total cholesterol
- HDL cholesterol
- Smoking
- Diastolic blood pressure

ASCVD POOLED COHORT EQUATION (PCE)

- Age
- Race
- Smoking
- Diabetes
- HDL cholesterol
- Total cholesterol
- Gender
- Systolic blood pressure
- Receiving treatment for high blood pressure

Currently, CVD is detected using several tests:

Exercise ECG

Measures the electrical activity of the heart during physical activity

Cardiac Catheterization

A thin, flexible tube is inserted into an artery or vein and guided to the heart

Echocardiography

Ultrasound-based imaging technique that creates detailed pictures of the heart's structure and function

CCTA

Imaging technique that uses X-rays and contrast material to visualize the coronary arteries

Single-Photon Emission Computed Tomography (SPECT)

Nuclear imaging technique that uses radioactive tracers to generate 3D images of blood flow to the heart

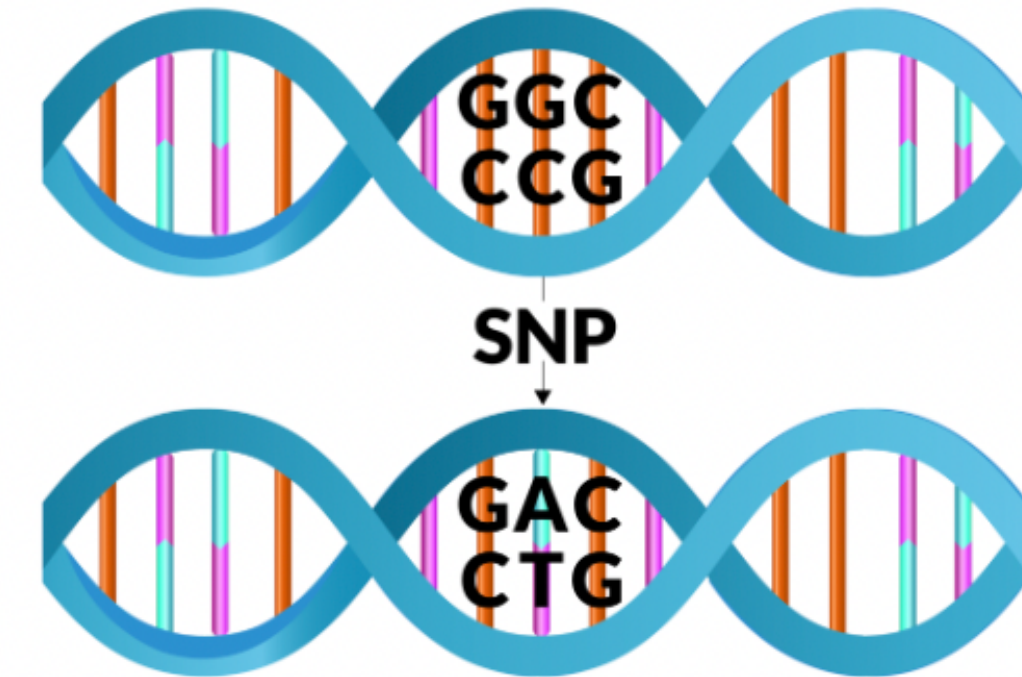
Cardiac Magnetic Resonance Imaging

Uses powerful magnets and radio waves to create detailed images of the heart's structure and function

Two Types of DNA Biomarkers Power Our Approach

GENETICS (SINGLE NUCLEOTIDE POLYMORPHISMS)

- Inherited from parents
- <20% of risk for cardiovascular disease is driven by genetics⁽¹⁾
- Does not change over time (i.e., not dynamic)



EPIGENETICS (DNA METHYLATION)

- Influenced by lifestyle & environment
- Larger driver of risk for cardiovascular disease as compared to genetics
- Largely confounded by genetics
- Changes over time (i.e., dynamic) (similar to HbA1c)

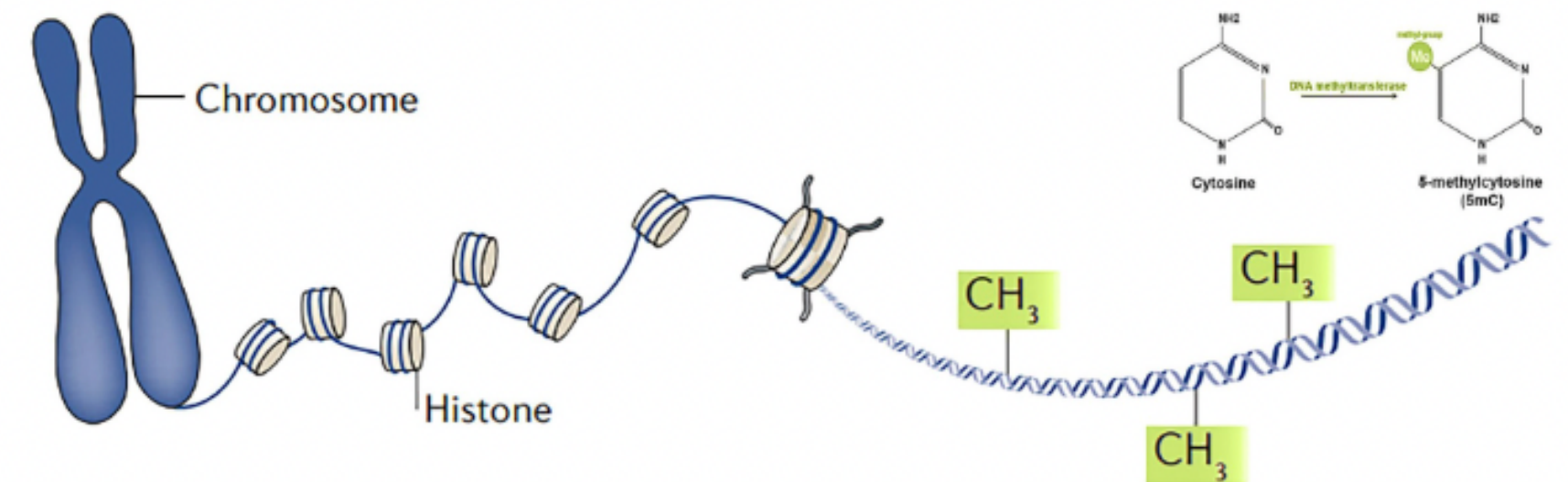
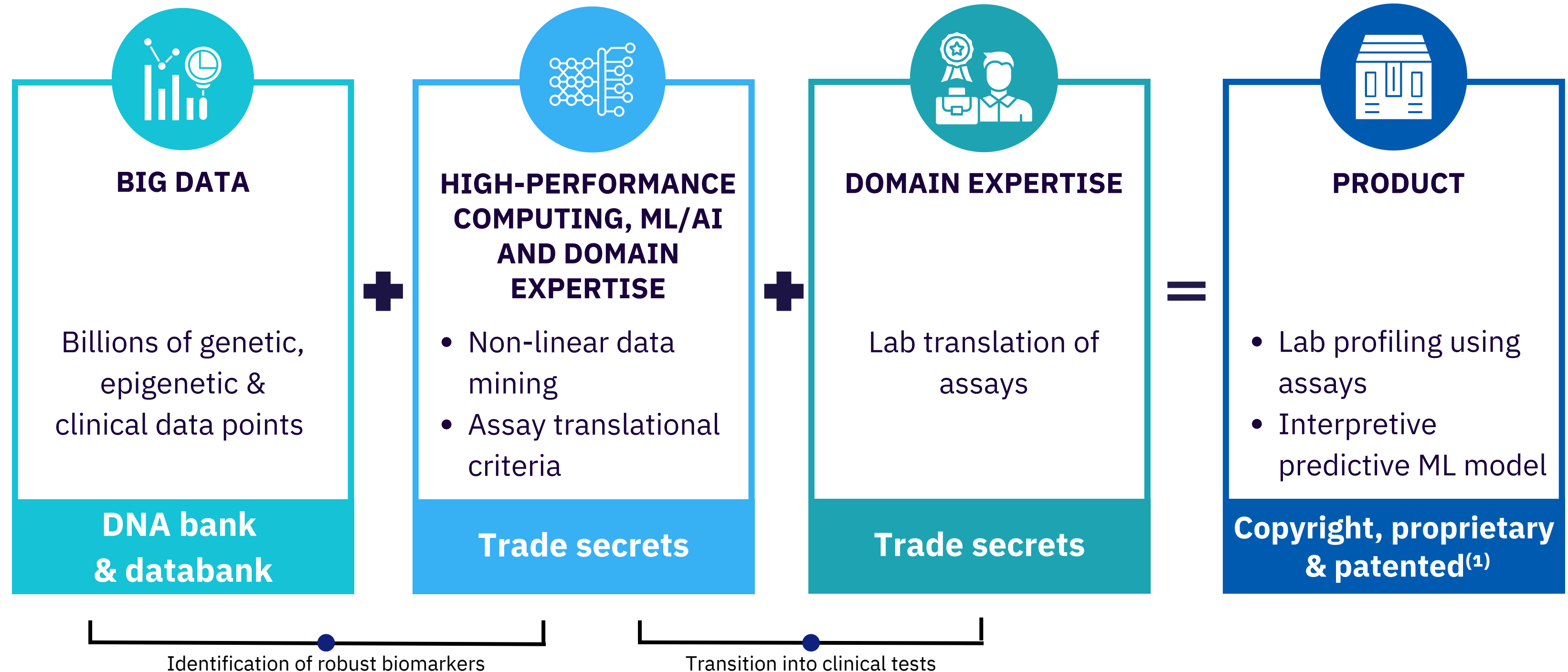


Fig 1. DNA methylation (5mC) ⁽²⁾

Our AI-Driven Integrated Epigenetic-Genetic Engine™

Proprietary Engine designed and built over the past decade



Our AI-Driven Integrated Epigenetic-Genetic Engine™ enables rapid design, development and launch of new diagnostic solutions

Cardio Diagnostics' Suite of Solutions



Epi+Gen CHD™

Only epigenetics-based test in the world for coronary heart disease risk assessment

It is a more sensitive and non-invasive alternative to the Framingham Risk Score (FRS), and the Atherosclerotic Cardiovascular Disease (ASCVD) Risk Calculator for predicting the three-year-risk for coronary heart disease.



Actionable Clinical Intelligence™

A one-of-a-kind platform that offers new epigenetic and genetic insights to clinicians prescribing the Epi+Gen CHD™ and PrecisionCHD™ tests



PrecisionCHD™

Only epigenetics-based test in the world for coronary heart disease detection

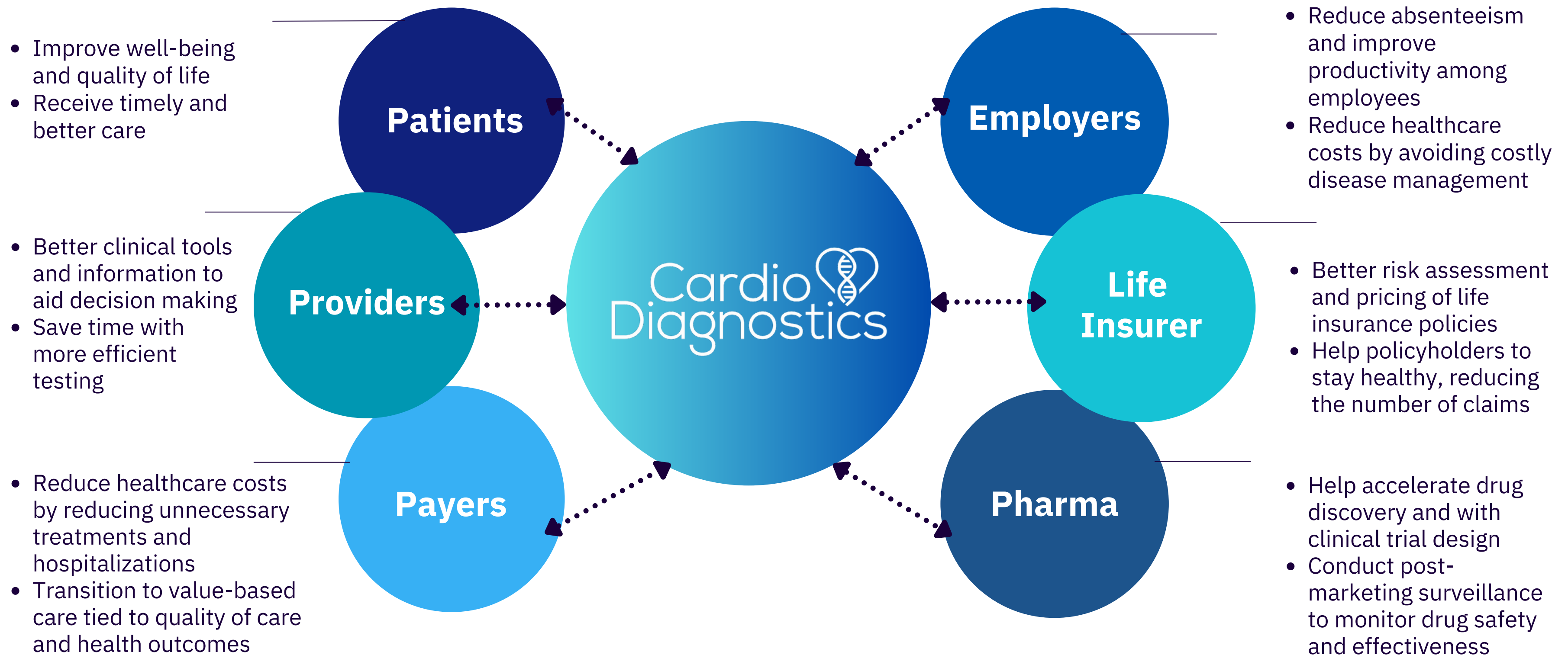
It is a sensitive and non-invasive alternative to exercise stress tests, nuclear stress tests, stress echocardiograms, coronary angiograms, and cardiac catheterization for evaluating coronary heart disease.









CardioInnovate360™

Research-use-only (RUO) solution to support the discovery, development and validation of novel biopharmaceuticals for the assessment and management of cardiovascular diseases

Our Differentiated Solutions Address the Needs of Major Healthcare Stakeholders



Clear, Key Differentiations for Coronary Heart Disease

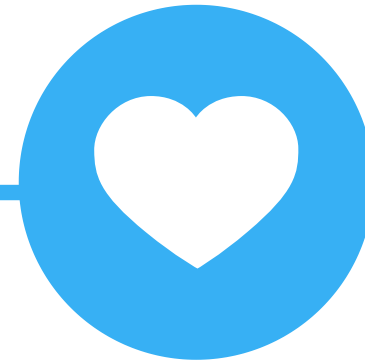
		Hospitals & Clinics					
SENSITIVE EPIGENETICS BASED TEST	✓	✗	✗	✗	✗	✗	✗
CORONARY HEART DISEASE SPECIFIC	✓	✓	✗	✓	✗	✗	✓
PHYSICIAN ORDERED AND/OR INTERPRETED	✓	✓	✗	✓	✓	✗	✓
AT-HOME TESTING AVAILABLE	✓	✗	✓	✗	✓	✗	✗
MULTIPLE DNA BIOMARKERS-BASED TEST	✓	✗	✗	✗	✗	✗	✗
MONITOR TREATMENT RESPONSE ⁽¹⁾	✓	✗ ⁽²⁾	✗	✗	✗	✓	✗

Epi+Gen CHD™ and PrecisionCHD™: A \$185B US Total Addressable Market⁽¹⁾



We expect to accelerate the adoption of Epi+Gen CHD™ and PrecisionCHD™ across several channels including:

- Telemedicine
- Providers - concierge practices, innovative health systems
- Payers
- Employers
- Life insurers

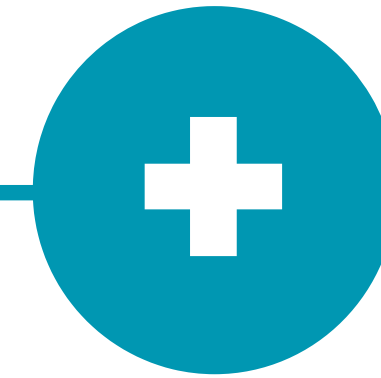


Epi+Gen CHD™ is recommended for:

- Adults ages 35-75
- Have not been diagnosed with coronary heart disease,
- Approximately 146M Americans⁽²⁾

PrecisionCHD™ is recommended for:

- Adults ages 35-80
- Presenting to be evaluated for coronary heart disease
- Approximately 157M Americans⁽²⁾



We intend to accelerate the adoption of both tests by:

- Developing strategic clinical partnerships
- Leveraging industry organizations
- Launching a piloting program
- Developing a customized customer portal to reduce transaction friction

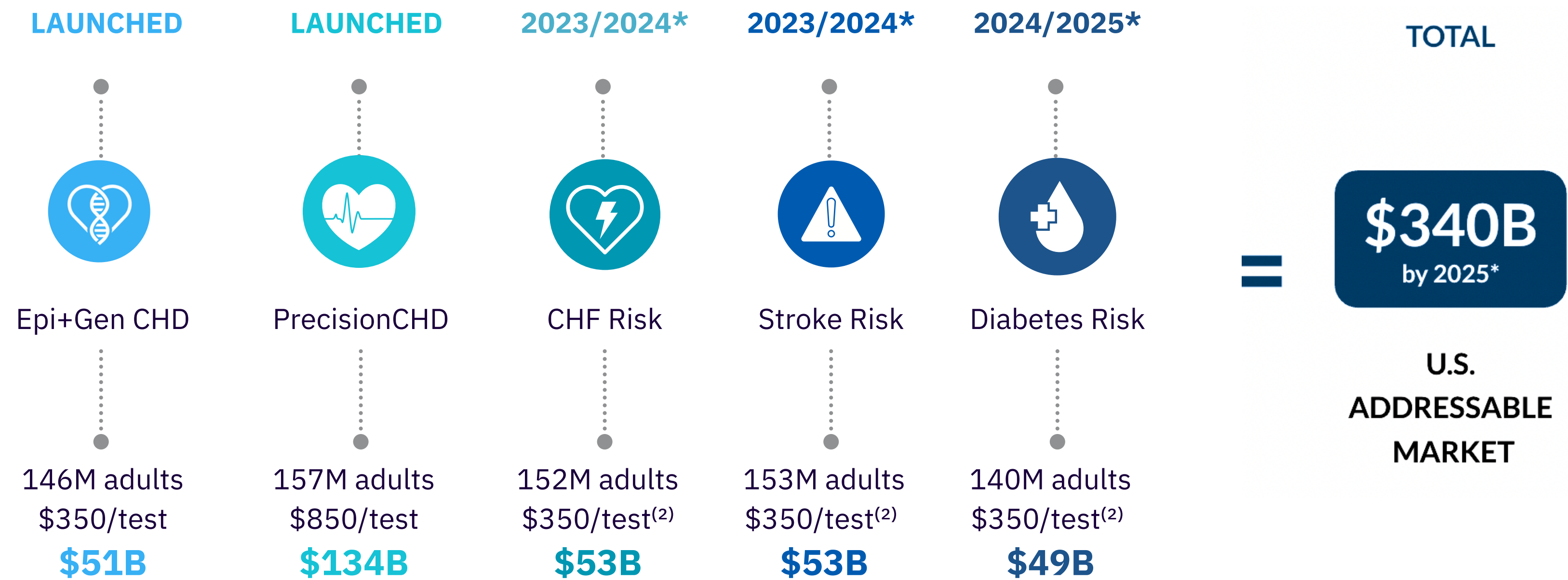
⁽¹⁾ Assumes 146M Americans x \$350/test for Epi+Gen CHD and assumes 157M Americans x \$850/test for PrecisionCHD

⁽²⁾ US Census Bureau

The Integrated Genetic-Epigenetic Engine™ Can be Leveraged Repeatedly

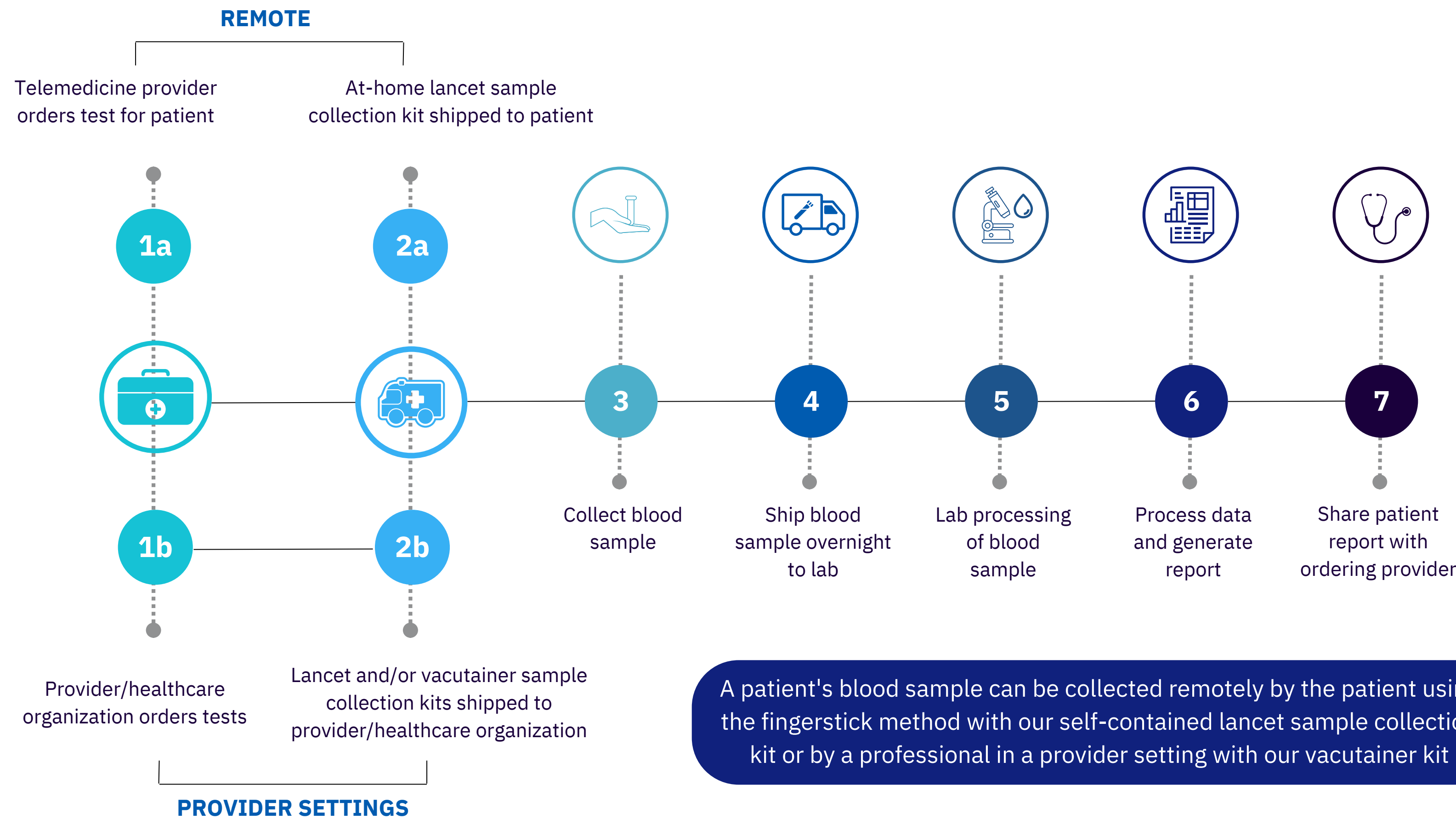
Assumes one patient could be tested with multiple tests⁽¹⁾

*Represents expected launch date

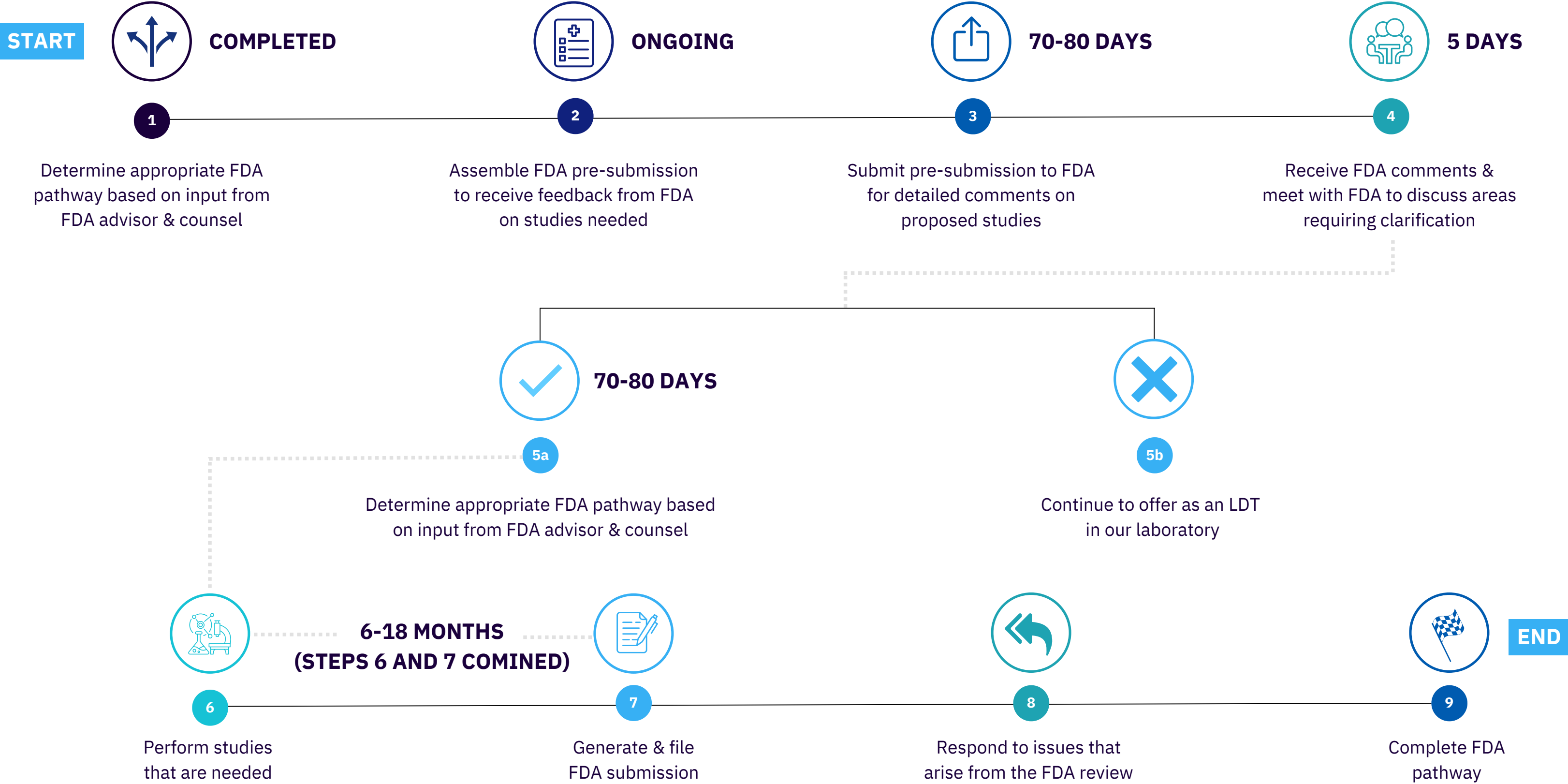


Source: Cardio Diagnostics estimate for US market based on 2020 US Census datas
⁽¹⁾ Assumes each test is administered to each patient a single time in a year although some patients may be eligible to be re-tested in less than a year
⁽²⁾ Assumed price per test

A Scalable Testing & Reporting Process to Fulfill Increasing Demand



FDA Regulatory Pathway Enables More Labs to Process Tests



As Laboratory Developed Test (LDTs)⁽¹⁾, Epi+Gen CHD™ and PrecisionCHD™ presently do not require FDA premarket authorization. Cardio Diagnostics is evaluating an FDA regulatory pathway to enable broader access to our tests.

⁽¹⁾ There is currently pending legislation in Congress intended to give authority to FDA to regulate certain types of LDTs including a bill that has moved recently out of committee to the full Senate for consideration.



⁽¹⁾ KOLs: Key Opinion Leaders

Robust Short-Term & Long-Term Strategic Initiatives

GROWTH STRATEGIES	INCREASE REVENUE	MANAGE RISKS	REDUCE VARIABLE COSTS
INTERNAL LAB	✓	✓	✓
PURSUE FDA PATHWAY	✓	✓	✓
PAYOR COVERAGE	✓	✓	
TARGET MULTIPLE REVENUE CHANNELS	✓	✓	
LAUNCH MULTIPLE SYNERGISTIC PRODUCTS	✓	✓	

Strong Leadership

Experienced leadership, complementary backgrounds & vision to succeed.



Warren Hosseinion, MD

Chairman

President, Nutex Health, Inc. (NUTX) - \$407M market cap⁽¹⁾
Co-founder of Apollo Medical Holdings (AMEH) - \$1.59B market cap⁽¹⁾
Director and former CEO of Clinigence Holdings (CLNH)
MD from Georgetown University School of Medicine



Meesha Dogan, PhD

CEO, Co-Founder, & Director

12+ years bridging engineering, AI, and medicine,
Co-inventor of the Integrated Genetic-Epigenetic Engine™
PhD in Biomedical Engineering from the University of Iowa

Team Continued



Robert Philibert, MD PhD

CMO, Co-Founder & Director

15+ years in epigenetics and clinical translation
Co-inventor of the Integrated Genetic-Epigenetic Engine™
MD & PhD in Neuroscience from the University of Iowa



Elisa Luqman, JD MBA

CFO

Chief Legal Officer (SEC), Nutex Health, Inc. (NUTX)
Co-founder of bigVault Storage Technologies (acquired)
JD & MBA in Finance from Hofstra University
Licensed in NY/NJ and FL Corp Counsel

Team Continued



Tim Dogan, PhD

CTO

12+ years in high performance computing systems
Co-inventor of the Integrated Genetic-Epigenetic Engine™
PhD in Mechanical Engineering from the University of Iowa



Khullani Abdullahi, JD

VP of Revenue & Strategy

13+ years in commercializing complex technologies and solutions
Growth architect at GreenLight Medical/Symplr, Lumere/GHX
JD from the University of Minnesota

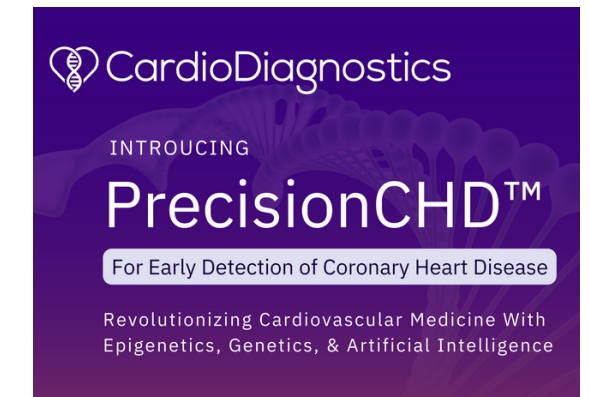
Achieved and Upcoming Milestones

• Completed Q1 - Q3 (as of 09/07/2023) milestones

- Partnerships with concierge and executive practices
- Launch of second test, PrecisionCHD™, for the detection of coronary heart disease
- Notice of allowance of patents in China and Australia
- Dr. Damon Broyles, VP of Clinical Innovation at Mercy Technology Services, joined as strategic advisor for precision cardiovascular medicine strategy
- Financing agreement with Yorkville Advisors Global, LP
- Launch of CardioInnovate360™, a biopharma research system to aid with the discovery, development and validation of novel biopharmaceuticals
- Partnership with Connect Clinic, a mobile health clinic, to help MidWest/South Central self-insured employers build access to heart disease initiatives
- Launch of Actionable Clinical Intelligence™, a provider-facing platform to provide personalized insights for coronary heart disease management
- Go-to-market expansion into the employer vertical with a focus on self-insured employers: FRSTeam heart disease fair and Truckers Health Network
- Peer-reviewed publications and study in partnership with Ascension Borgess Hospital's Heart Attack Prevention Clinic

• Expected 2023 (09/07/2023 onwards) milestones

- Complete ongoing health economic study for PrecisionCHD™
- Publish PrecisionCHD™ validation study completed in collaboration with Intermountain Healthcare and University of Iowa Hospitals and Clinics
- Announcements of additional product launches
- Announcements of additional studies
- Announcements of additional strategic partnerships/customers



Risk Factors

Our business is subject to numerous risks and uncertainties, including those highlighted in the section titled “Risk Factors,” that represent challenges that we face in connection with the successful implementation of our strategy and growth of our business. The occurrence of one or more of the events or circumstances described in the section titled “Risk Factors,” alone or in combination with other events or circumstances, may adversely affect our ability realize the anticipated benefits of the Business Combination, and may have an adverse effect on our business, cash flows, financial condition and results of operations. Such risks include, but are not limited to:

Risks Related to Cardio’s Business, Industry and Business Operations

- We have a limited operating history that makes it impossible to reliably predict future growth and operating results.
- We have an unproven business model, have not generated significant revenues and can provide no assurance of generating significant revenues or operating profit.
- The market for epigenetic tests is fairly new and unproven, and it may decline or experience limited growth, which would adversely affect our ability to fully realize the potential of our business plan.
- The estimates of market opportunity and forecasts of market growth included in this Annual Report on Form 10-K may prove to be inaccurate, and even if the market in which we compete achieves the forecasted growth, our business could fail to grow at similar rates, if at all.
- If we are not able to enhance or introduce new products that achieve market acceptance and keep pace with technological developments, our business, results of operations and financial condition could be harmed.
- The success of our business depends on our ability to expand into new vertical markets and attract new customers in a cost-effective manner.
- Our growth strategy may not prove viable and expected growth and value may not be realized.
- Our future growth could be harmed if we lose the services of our key personnel.
- We may face intense competition, which could limit our ability to maintain or expand market share within our industry, and if we do not maintain or expand our market share, our business and operating results will be harmed.
- Our business depends on customers increasing their use of our existing and future tests, and we may experience loss of customers or a decline in their use of our solutions.
- We rely on a limited number of suppliers, contract manufacturers, and logistics providers, and our test is performed by a single contract high complexity Clinical Laboratory Improvement Amendments (CLIA) laboratory.
- We may be unable to scale our operations successfully.
- We may be unable to manage our growth.
- Our success depends upon our ability to adapt to a changing market and our continued development of additional tests and services.
- Our Board of Directors may change our strategies, policies, and procedures without stockholder approval.
- We may need to seek alternative business opportunities and change the nature of our business.
- We are subject to general litigation that may materially adversely affect us and our operations.

Risks Related to Cardio’s Intellectual Property

- Certain core technology of Cardio is licensed, and that license may be terminated if Cardio were to breach its obligations under the license.
- Cardio’s license agreement with University of Iowa Research Foundation (UIRF) includes a non-exclusive license of “technical information” that potentially could grant unaffiliated third parties access to materials and information considered derivative work made by Cardio, which could be used by such licensees to develop competitive products.

Risk Factors



Risks Related to Government Regulation

- Cardio conducts business in a heavily regulated industry, and if it fails to comply with these laws and government regulations, it could incur penalties or be required to make significant changes to its operations or experience adverse publicity, which could have a material adverse effect on its business, financial condition, and results of operations.
- If the FDA were to begin actively regulating Cardio’s tests, Cardio could incur substantial costs and delays associated with trying to obtain premarket clearance or approval and incur costs associated with complying with post-market controls.
- If Cardio’s products do not receive adequate coverage and reimbursement from third-party payors, its ability to expand access to its tests beyond its initial sales channels will be limited and its overall commercial success will be limited.

Risks Related to the Business Combination and being a Public Company

- Going public through a merger rather than an underwritten offering presents risks to unaffiliated investors. Subsequent to our completion of the Business Combination, we may be required to take write-downs or write-offs, restructuring and impairment or other charges that could negatively affect our financial condition, results of operations and stock price, which could cause you to lose some or all of your investment.
- Our management will be required to devote substantial time to maintaining and improving its internal controls over financial reporting and the requirements of being a public company which may, among other things, strain our resources, divert management’s attention and affect our ability to accurately report our financial results and prevent fraud.
- We will need to grow the size of our organization and may experience difficulties in managing this growth.
- Because substantially all of the shares eligible for redemption in connection with the Business Combination were redeemed, our stock may become less liquid following the Business Combination.
- Because substantially all of the shares eligible for redemption in connection with the Business Combination were redeemed, the trust account that held proceeds from the Mana IPO was nearly exhausted paying the redemption amount, leaving very little cash for funding future operations and opening the possibility that we will need to raise additional capital sooner than we had anticipated prior to the Business Combination.
- Our stockholders prior to the Business Combination (“Mana Stockholders”) will experience immediate dilution as a consequence of the issuance of new shares to the Legacy Cardio stockholders and equity rights holder as consideration in the Business Combination. Having a minority share position may reduce the influence that Mana Stockholders have on the management of our company.

Risks Related to Cardio's Common Stock

- The price of our Common Stock likely will be volatile like the stocks of other early-stage companies.
- Because nearly 50% of our currently outstanding shares of Common Stock are registered for resale, we may have difficulty raising additional capital when and if needed.
- A significant number of shares of our Common Stock are subject to issuance upon exercise of outstanding warrants and options, which upon such exercise may result in dilution to our security holders.
- We have never paid dividends on our Common Stock, and we do not anticipate paying any cash dividends on our Common Stock in the foreseeable future.
- Sales of a substantial number of shares of our Common Stock in the public market by our existing stockholders could cause our stock price to decline.
- Insiders will continue to have substantial influence over the Company after the Business Combination, which could limit investors’ ability to affect the outcome of key transactions, including a change of control.

Risks Related to Financing with Recent Financing

- Future sales of Common Stock in the public market could cause our share price to decline significantly, even if our business is doing well.
- We may issue additional shares of our Common Stock or other equity securities without your approval, which would dilute your ownership interests and may depress the market price of our Common Stock.
- A significant number of shares of our Common Stock are subject to issuance upon exercise of outstanding warrants and options and conversion of Convertible Debentures, which upon such exercise or conversion, as the case may be, may result in dilution to our security holders.

*An extensive list of factors that can affect future results are discussed in the Current Report on Form 10-K for the period ended December 31, 2022 and 10-Q for the period ended March 31, 2023 under the heading “Risk Factors” in Part I, Item 1A thereof, and other documents filed from time to time with the Securities and Exchange Commission. Such factors could materially adversely affect the Company's financial performance and could cause the Company's actual results for future periods to differ materially from any opinions or statements expressed within this presentation.

For more information,
please email:



investors@cardiodiagnosticsinc.com

Cardio Diagnostics

Revolutionizing Cardiovascular
Medicine With Epigenetics & AI



APPENDIX

 CardioDiagnostics
Revolutionizing Cardiovascular Medicine
With Epigenetics and AI



Cardiovascular Disease and Associated Co-Morbidities

In the US, nearly 18 million Americans have some type of cardiovascular disease (CVD), and CVD is responsible for both 1 in every 4 deaths and nearly \$1 billion/day in medical costs + lost productivity.⁽¹⁾⁽²⁾

CORONARY HEART DISEASE (CHD)

The most common type of CVD



- 20+ million adults have CHD, the major cause of heart attacks⁽²⁾
- A heart attack occurs every 40 seconds⁽²⁾
- 800,000+ heart attacks / year⁽²⁾

STROKE

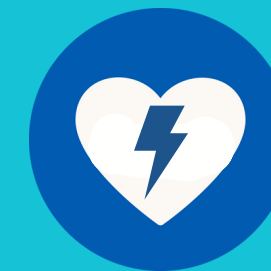
A common type of CVD



- Nearly 800,000 strokes each year⁽²⁾
- A stroke-related death occurs every 3.5 minutes⁽²⁾
- 1 in 6 CVD-related deaths are due to stroke⁽²⁾

CONGESTIVE HEART FAILURE (CHF)

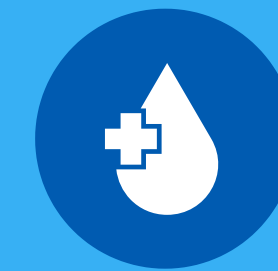
A common type of CVD



- 6+ million adults have heart failure⁽²⁾
- Nearly 380,000 deaths in 2018 were attributed to heart failure⁽²⁾

DIABETES

A major risk factor for CVD



- 34+ million adults have diabetes⁽³⁾
- 2-4x more likely to develop CVD⁽⁴⁾

Epi+Gen CHD™: The *Only* Epigenetics-Based Test For Coronary Heart Disease Risk Assessment

- Epi+Gen CHD™ is Cardio Diagnostics' first product that was developed using our AI-driven Integrated Genetic-Epigenetic Engine™ and was validated in collaboration with Intermountain Healthcare.
- Epi+Gen CHD™ is a powerful test that combines epigenetics, genetics and artificial intelligence to **predict 3-year risk for coronary heart disease** (CHD), the most common type of heart disease and the major cause of heart attacks.
- Epi+Gen CHD™ addresses the shortcomings of current risk assessment tests because it:
 - Demonstrated strong clinical value with **76% sensitivity for men and 78% sensitivity for women**, which is **1.7 times and 2.4 times more sensitive for men and women**, respectively, compared to the average sensitivity of FRS and PCE⁽¹⁾ ⁽²⁾
⁽³⁾
 - Demonstrated strong economic value showing up to **\$42,000 in cost savings per quality adjusted life year** and improved survival ⁽⁴⁾
 - Is a simple, non-invasive blood test performed in a high complexity CLIA lab
 - **Sample can be collected at-home or in provider settings**
 - **Does not require fasting or depend on self-reported information**
 - Is coupled to Cardio Diagnostics' Actionable Clinical Intelligence™ platform to assist clinicians in **personalizing clinical decisions**



PrecisionCHD™: The *Only* Epigenetics-Based Test For Coronary Heart Disease Detection

- PrecisionCHD™ is Cardio Diagnostics' second product that was developed using our AI-driven Integrated Genetic-Epigenetic Engine™ and was validated in collaboration with Intermountain Healthcare and University of Iowa Hospitals and Clinics.
- PrecisionCHD™ is a powerful test that combines epigenetics, genetics and artificial intelligence to **assess the presence of coronary heart disease** (CHD), the most common type of heart disease and the major cause of heart attacks.
- PrecisionCHD™ addresses the shortcomings of current detection tests because it:
 - Demonstrated strong clinical value with **80% sensitivity for men and 76% sensitivity for women, compared to the sensitivity of exercise ECG of 45-68%** ^{(1) (2) (3)}
 - Is a simple, non-invasive blood test performed in a high complexity CLIA lab
 - **Sample can be collected at-home or in provider settings without the need to wait weeks or months to get tested**
 - **Does not** require preparation or exposure to radiation
 - Is coupled to Cardio Diagnostics' Actionable Clinical Intelligence™ platform to assist clinicians in **personalizing clinical decisions**
- Multiple compelling clinical and economic studies to expand evidence dossier are in progress



⁽¹⁾ This means that for every 100 men and 100 women deemed "have" CHD, the test correctly identifies 80 men & 76 women

⁽²⁾ Philibert R et al., 2023, In Submission

⁽³⁾ Morrow D et al., 2018, A Textbook of Cardiovascular Medicine

Actionable Clinical Intelligence™: Assisting Clinicians in Personalizing Clinical Decision Making

A rectangular graphic with a blue-to-purple gradient background. It features a faint, vertical pattern of binary code (0s and 1s) in the background. The text "Actionable Clinical Intelligence™" is centered in a white, sans-serif font.

Actionable Clinical Intelligence™

- A **one-of-a-kind platform** that offers new epigenetic and genetic insights to clinicians prescribing the Epi+Gen CHD™ and PrecisionCHD™ tests. These insights are:
 - Generated by integrating the test results with a patient's unique epigenetic and genetic biomarkers together with clinical information to provide **deeper and actionable insights** to clinicians about factors driving the patient's coronary heart disease
 - Are **tailored to each patient** to help elucidate areas of concern and aid a clinician's independent assessment, with the goal of improving patient outcomes
 - Include the **relative contribution** of each of the patient's biomarkers to CHD, evidence on the role of these biomarkers in **coronary heart disease pathogenesis**, and changes in the measured biomarkers over time in **response to lifestyle and therapeutic interventions**

Epi+Gen CHD™ and PrecisionCHD™ are the Next Generation Tests for Cardiovascular Medicine

Patient

- 35-75 years old
- Have not developed signs or symptoms associated with coronary heart disease (CHD)
- Have not been diagnosed with CHD
- Need to undergo testing for primary prevention of CHD



Without Epi+Gen CHD™

- Requires in-person clinic visit that may take days, weeks or months to complete
- Multiple tubes of blood needed to be collected in person for testing
- The average sensitivity of FRS & PCE was found to be 44% in men and 32% in women⁽¹⁾⁽²⁾
- Patient care plan lacks personalization



With Epi+Gen CHD™

- Can be completed remotely or in provider settings
- Simple blood test where lancet-based collection kit can be done at-home or vacutainer-based collection can be done in provider settings
- The average sensitivity was 76% for men and 78% sensitivity for women, which is 1.7 times and 2.4 times more sensitive for men and women, respectively
- Patient care plan highly personalizable with ACI™

Epi+Gen CHD™ and PrecisionCHD™ are the Next Generation Tests for Cardiovascular Medicine

Patient

- 35-80 years old
- Presenting to be evaluated for CHD
- Need to undergo testing for the detection of CHD



Without PrecisionCHD™

- Requires in-person clinic visit that may take days, weeks or months to complete
- Long testing duration and more invasive tests
- Exposure to ionizing radiation
- Patient management plan lacks personalization
- The sensitivity of exercise ECG for example is only 45-68⁽¹⁾

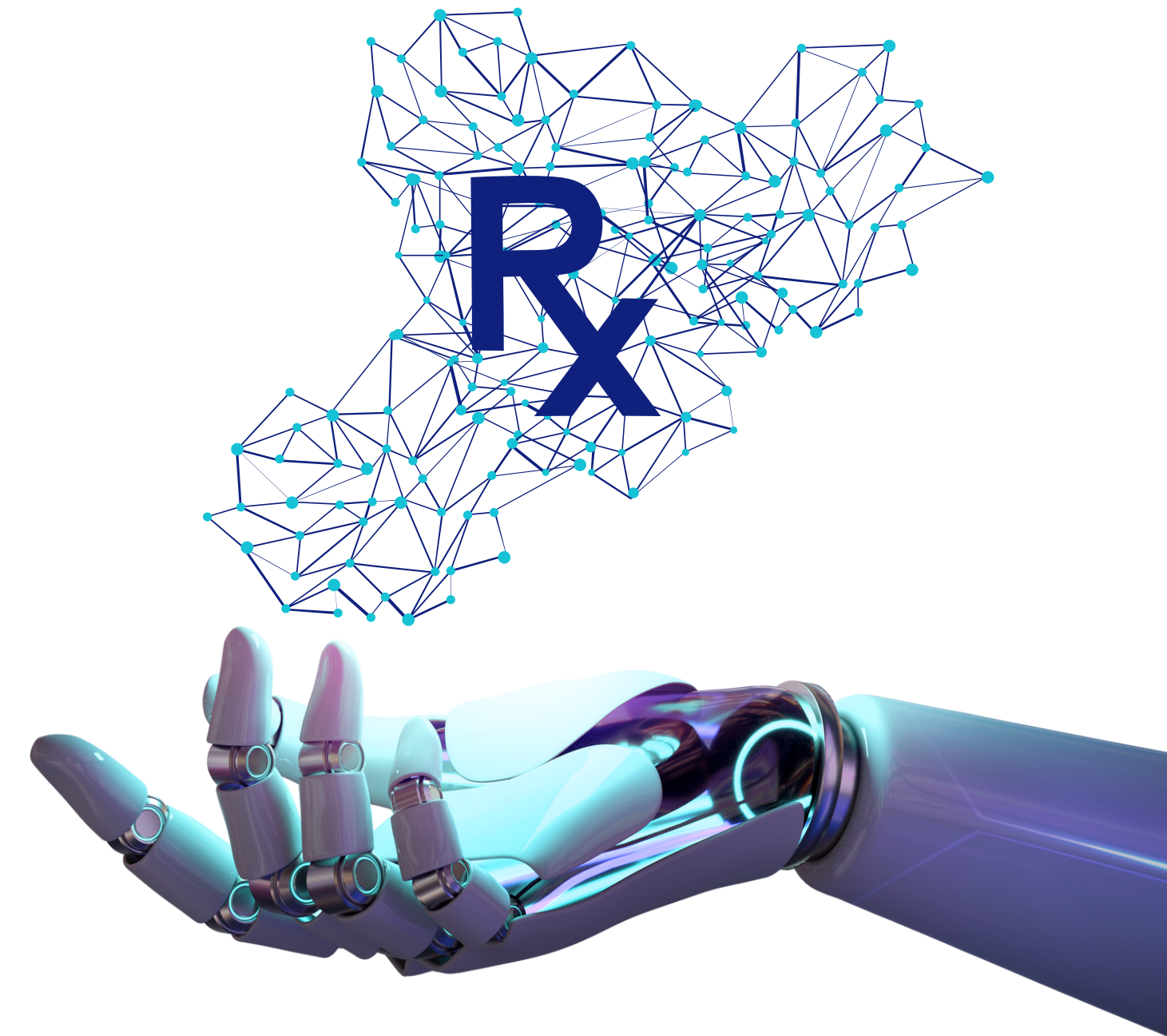


With PrecisionCHD™

- Can be completed remotely or in provider settings
- Simple blood test where lancet-based collection kit can be done at-home or vacutainer-based collection can be done in provider settings
- No exposure to ionizing radiation
- Patient care plan highly personalizable with ACI™
- The average sensitivity is 80% for men and 76% for women, compared to the sensitivity of exercise ECG of 45-68%⁽²⁾

CardioInnovate360™: A BioPharma Research System That Harnesses the Power of Epigenetics, Genetics and Artificial Intelligence

- CardioInnovate360™ is a research-use-only (RUO) solution to **support the discovery, development and validation of novel biopharmaceuticals** for the assessment and management of cardiovascular diseases
- Potential to provide a **new and non-reimbursement-dependent revenue stream** for Cardio Diagnostics
- Helps establish a footprint for the company in a **new market**
- Leverages, in part, Cardio Diagnostics' proprietary AI-Driven Integrated Genetic-Epigenetic Engine™ at scale to **help accelerate drug discovery, design clinical trials, conduct post-marketing surveillance, and develop custom applications**
- Example business model for this offering includes licensing, development services etc



Cardio Diagnostics' Solutions are Backed by Comprehensive Evidence that Matter to Healthcare Stakeholders



- Rigorous clinical and analytic validation of biomarkers and Artificial Intelligence models
 - Dogan et al, 2021, External Validation of Integrated Genetic-Epigenetic Biomarkers for Predicting Incident Coronary Heart Disease, Epigenomics (In collaboration with Intermountain Healthcare)
 - Philibert et al, 2021, The Reversion of DNA Methylation at Coronary Heart Disease Risk Loci in Response to Prevention Therapy, Processes
 - Analytical validation performed to meet Clinical Laboratory Improvement Amendment (CLIA) requirements
 - Philibert et al 2023, The Validation of an Integrated Genetic-Epigenetic Test for the Assessment of Coronary Heart Disease, In submission
 - Additional clinical studies are ongoing
- Health economic studies to demonstrate substantial savings and ROI
 - Jung et al, 2021, Cost–Utility Analysis of an Integrated Genetic-Epigenetic Test for Assessing Risk for Coronary Heart Disease, Epigenomics
 - Additional health economic studies are ongoing

Research Article

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External validation of integrated genetic-epigenetic biomarkers for predicting incident coronary heart disease

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Aim: The Framingham Risk Score (FRS) and ASCVD Pooled Cohort Equation (PCE) for predicting risk for incident coronary heart disease (CHD) poorly. To improve risk stratification for CHD, we developed a novel integrated genetic-epigenetic tool. **Materials & methods:** Using machine learning techniques and datasets from the Framingham Heart Study (FHS) and Intermountain Healthcare (IM), we developed and validated an integrated genetic-epigenetic model for predicting 3-year incident CHD. **Results:** Our approach was more sensitive than FRS and PCE and had high generalizability across cohorts. It performed with sensitivity/specificity of 79/75% in the FHS test set and 75/72% in the IM set. The sensitivity/specificity was 15/93% in FHS and 31/89% in IM for FRS, and sensitivity/specificity was 41/74% in FHS and 69/55% in IM for PCE. **Conclusion:** The use of our tool in a clinical setting could better identify patients at high risk for a heart attack.

Lay abstract: Current lipid-based methods for assessing risk for coronary heart disease (CHD) have limitations. Conceivably, incorporating epigenetic information into risk prediction algorithms may be beneficial, but underlying genetic variation obscures its effects on risk. In order to develop a better CHD risk assessment method, we used artificial intelligence to identify genome-wide genetic and epigenetic biomarkers from two independent datasets of subjects characterized for incident CHD. The resulting algorithm significantly outperformed the current assessment methods in independent test sets. We conclude that artificial intelligence-moderated genetic-epigenetic algorithms have considerable potential as clinical tools for assessing risk for CHD.

First draft submitted: 14 April 2021; Accepted for publication: 7 June 2021; Published online: 21 June 2021

Keywords: artificial intelligence • coronary heart disease • digital PCR • epigenetics • genetics • machine learning • prevention

Coronary heart disease (CHD) is the most common type of heart disease and was responsible for over 360,000 deaths in the USA in 2017 [1]. In order to decrease this recurring toll, a number of primary prevention risk estimators have been developed to better identify those at risk for CHD. Beginning with the Framingham Risk Score (FRS) and more recently, the ASCVD Pooled Cohort Equation (PCE), these risk stratification tools capture variance in key potentially treatable parameters, such as serum lipid levels, known to be associated with risk for CHD [2,3]. Despite the magnitude of these efforts, current risk scores often lack in sensitivity and specificity. As a result, there is a need for alternative primary prevention risk stratification approaches for CHD.

Some of the newer risk prediction strategies take advantage of the rapid advancements in assessing genome-wide genetic or transcriptional variation [4–7]. Though each of these newer approaches has had some success, to date, their clinical impact has been limited. In particular, those algorithms relying only on genetic information have a

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Research Article

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Cost–utility analysis of an integrated genetic/epigenetic test for assessing risk for coronary heart disease

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Aim: New epigenetically based methods for assessing risk for coronary heart disease may be but are generally more costly than current methods. To understand their potential impact spending, we conducted a cost–utility analysis. **Methods:** We compared costs using the n CHD™ test with those of existing tests using a cohort Markov simulation model. **Results:** Use of the new test was associated with both better survival and highly competitive negative cost-effectiveness ratios ranging from -\$42,000 to -\$8000 per quality-adjusted life year for and without a secondary test. **Conclusion:** The new integrated genetic/epigenetic test w and lives under most real-world scenarios. Similar advantages may be seen for other epi

First draft submitted: 10 January 2021; Accepted for publication: 3 February 2021; Publish 24 February 2021

Keywords: coronary heart disease • cost–utility analysis • DNA methylation • economics • epigen medicine

The spiraling cost of healthcare has increased the need for better prevention strategies for co illnesses such as diabetes and heart disease. In particular, there have been repeated calls for be for use in preventative interventions [1,2]. Prior to the completion of the human genome sequen majority of the biomarker discovery efforts employed metabolomic or proteomic methods to ide markers [3]. Since then, scientists have complemented these earlier approaches by incorporating genotyping methods to identify genetic variations predictive of disease onset and severity [4]. De promise of these nucleic acid technologies, the impact of genetic approaches for identifying clinic biomarkers predictive of risk for illnesses such as heart disease has been limited [5,6]. Instead, due to t cost-to-information content ratio of the genetics-based approaches, clinicians continue to rely on r proteomic-based approaches for assessing risk of onset of syndromes, such as coronary heart disea whose management constitutes the bulk of day-to-day clinical interactions for primary care practi

Recent advances in epigenetics have opened yet another frontier for developing clinical bio in assessing the risk or presence of common syndromes. In particular, the US FDA's 2014 approval o a test that uses a combination of genetic, epigenetic and proteomic tests to assess the presence of colon cancer, has alerted both clinicians and healthcare payers to the potential of epigenetic testing technologies [7]. The test, which uses stool as its starting biomaterial, was used to screen 456,000 patients in the third quarter of 2019, with the cost being covered by major payers in the USA, including Medicare [8]. While it was the first to market, this epigenetically based test will not be the last; Taryma-Lesniak *et al.* recently reviewed the landscape of *in vitro* diagnostic tests and found 25 tests [6].

Understanding the importance o epigenetically oriented tests are to clinicians are responsible for orderin the test to the management of their the performance of the test will either market share (in the case of comm

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Circulation

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ABSTRACT

Tools Share

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Abstract

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HEALTH TECH

SESSION TITLE: HEALTH TECH POSTERS III

Abstract 13530: Epi+Gen CHD: A More Sensitive and Cost-Effective Tool to Assess Risk and Monitor Treatment Response for Coronary Heart Disease

Meeshe Dogan, Willem Philibert, Younsoo Jung, Tim Dogan, David Frisvold, Allan Andersen, Eric Hoffman and Robert Philibert

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Abstract

Coronary heart disease (CHD) is preventable, but current lipid-based risk assessment tools such as The Framingham Risk Score (FRS) and ASCVD Pooled Cohort Equation (PCE) have limitations. Using DNA-based genetic and epigenetic biomarkers, we have developed a more sensitive and cost-effective incident CHD risk assessment tool, Epi+Gen CHD, that can provide actionable insights and monitor treatment response. This test can be administered remotely via telemedicine using at-home sampling, or in a clinical setting. Epi+Gen CHD was developed and validated using

SAMPLE COLLECTION KIT CONTENTS & ASSEMBLY

- Common kit contents that can be sourced from multiple distributors
- Identified multiple distributors to diversify supply chain
- Most kit contents are shelf-stable for years and can be sourced well in advance
- Maintain inventory of fully assembled kits to meet six months of expected demand
- Assembly does not require special protocol
- Assembly & fulfillment of sample collection kits integrated internally

LABORATORY STRATEGY

- Favorable agreement in place with an experienced laboratory
- Refine plan to meet sample processing demand for at least 18 months
- Identified lead times of key suppliers to allow seamless capacity expansion as demand accelerates
- Intend to acquire or set up a laboratory to allow processing of patient samples internally

Gross Margin Expansion Opportunity

1

Potential lab
acquisition or set up



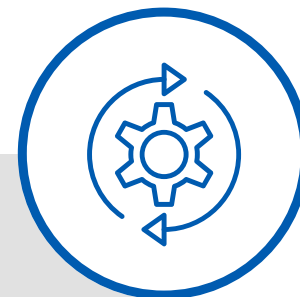
2

Process larger sample
batches



3

Increase processing
automation



4

Bulk shipping of
sample collection kits
and/or samples



Product and Company Recognitions



Winner
Biotech Innovation Showcase Award 2019



AACC
Disruptive Technology Award
Semifinalist⁽¹⁾