COMPANY UPDATE

MAY 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.

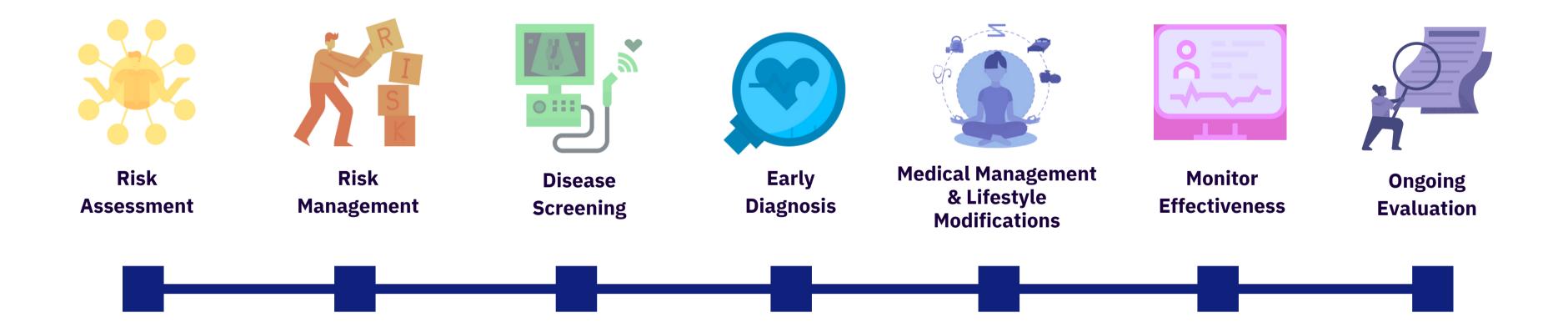
Key Investment Highlights

- NASDAQ listed: CDIO market cap \$19 million as of 5/15/2023
- 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

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.



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.

- cardiovascular diseases.

- market segments.

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DIVERSIFICATION

PRODUCTS

• Multiple launched and in development synergistic clinical and non-clinical products addressing various

• 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

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

OPERATIONS

SCALE

- 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.

- companies.
- new customers.



EXPERIENCE

CLINICAL

• Has profound understanding of clinical needs, challenges and opportunities.

• Deep expertise in designing, executing ad 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

• Experience expanding into new markets and targeting

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

#1	Cardiovascular disease (CVD) is t accounting for nearly 19 million d global deaths ⁽¹⁾
\$47 TRILLION LOSS	Globally, cardiovascular disease i output loss of \$47 trillion from 20 productivity losses, representing
72%	Following a healthy lifestyle may related to heart disease ⁽³⁾



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the leading cause of death globally, deaths per year, or about 32% of all

is expected to result in a cumulative 2011 to 2030 due to medical costs and g 75% of the global GDP in 2010 ^{(2) (3)}

prevent 72% of premature deaths

Cardiovascular Disease is a Burden for All Major Stakeholders



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⁾



Patients

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



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





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⁾

Life Insurers

Four Strategic Steps to Realize Our Vision



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



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

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



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

Echocardiography

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

Single-Photon Emission Computed Tomography (SPECT)

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

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Cardiac Catheterization

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

ССТА

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

Cardiac Magnetic Resonance Imaging

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

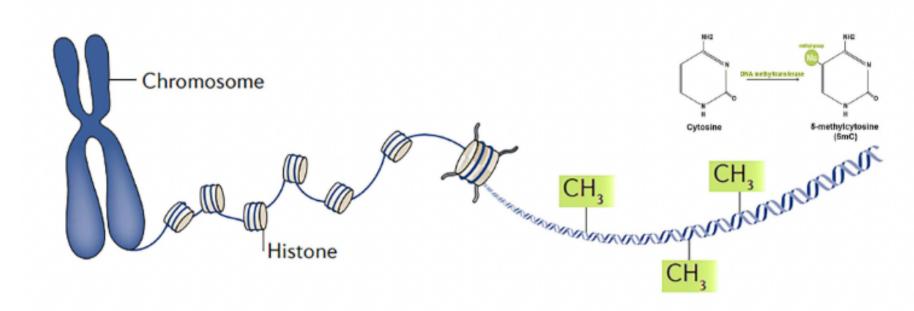
Two Types of DNA Biomarkers Power Our Approach

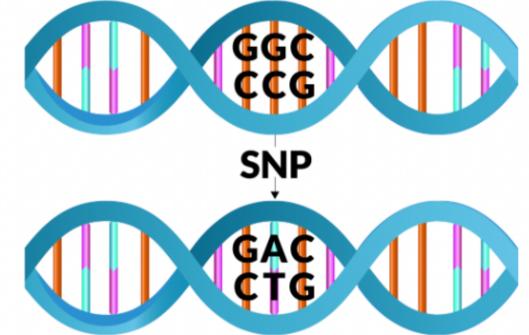
GENETICS (SINGLE NUCLEOTIDE POLYMORPHISMS)

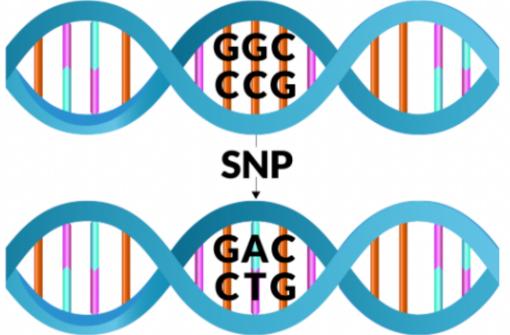
- Inherited from parents
- <20% of risk for cardiovascular disease is driven by genetics⁽¹⁾
- Does not change over time (i.e., not dynamic)

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)





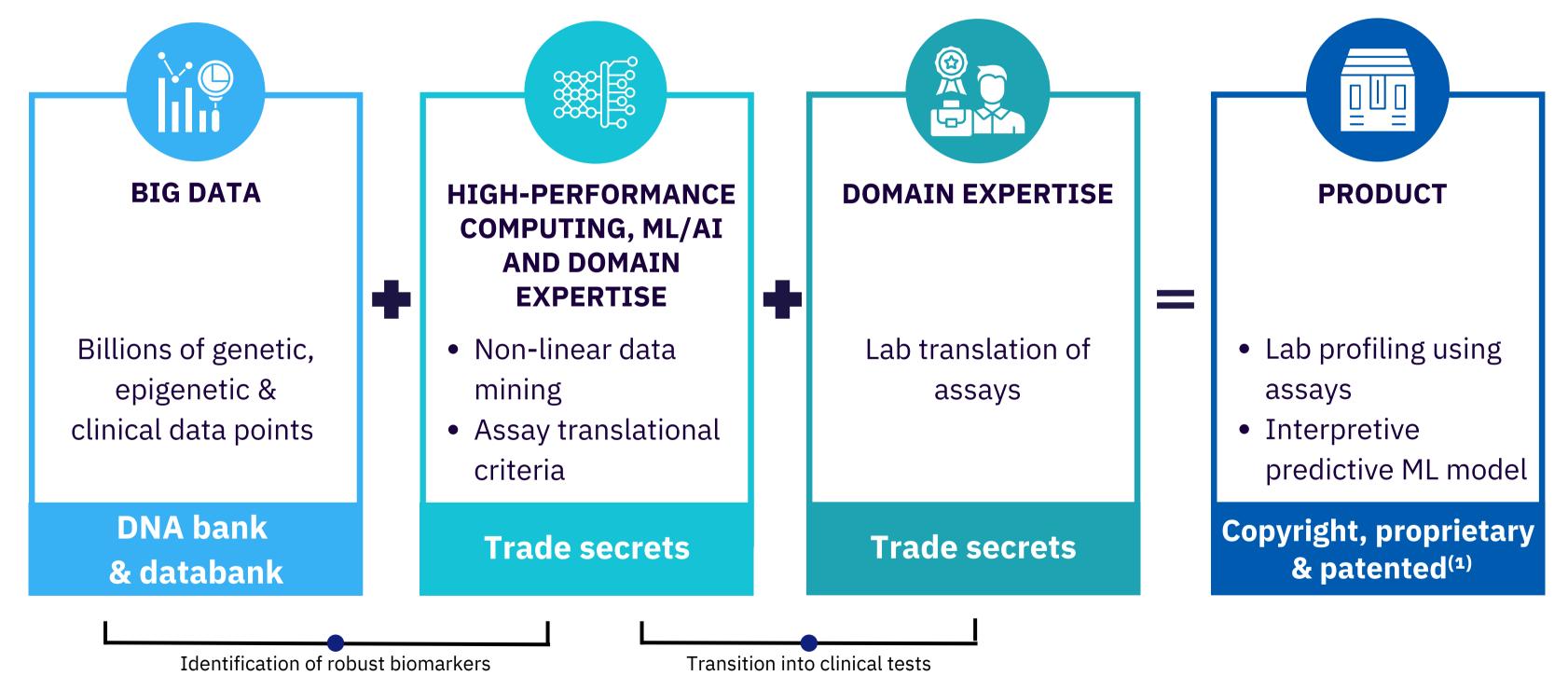


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Fig 1. DNA methylation (5mC)⁽²⁾

Our AI-Driven Integrated Epigenetic-Genetic Engine™

Proprietary Engine designed and built over the past decade



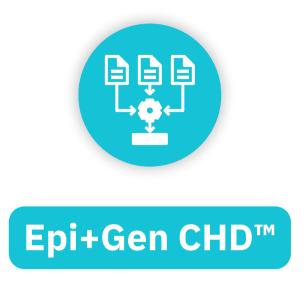
Our AI-Driven Integrated Epigenetic-Genetic Engine™ enables rapid design, development and launch of new diagnostic solutions



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⁽¹⁾ Patent granted 8/16/2022; Other patents pending

Cardio Diagnostics' Suite of Solutions



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. 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.



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



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

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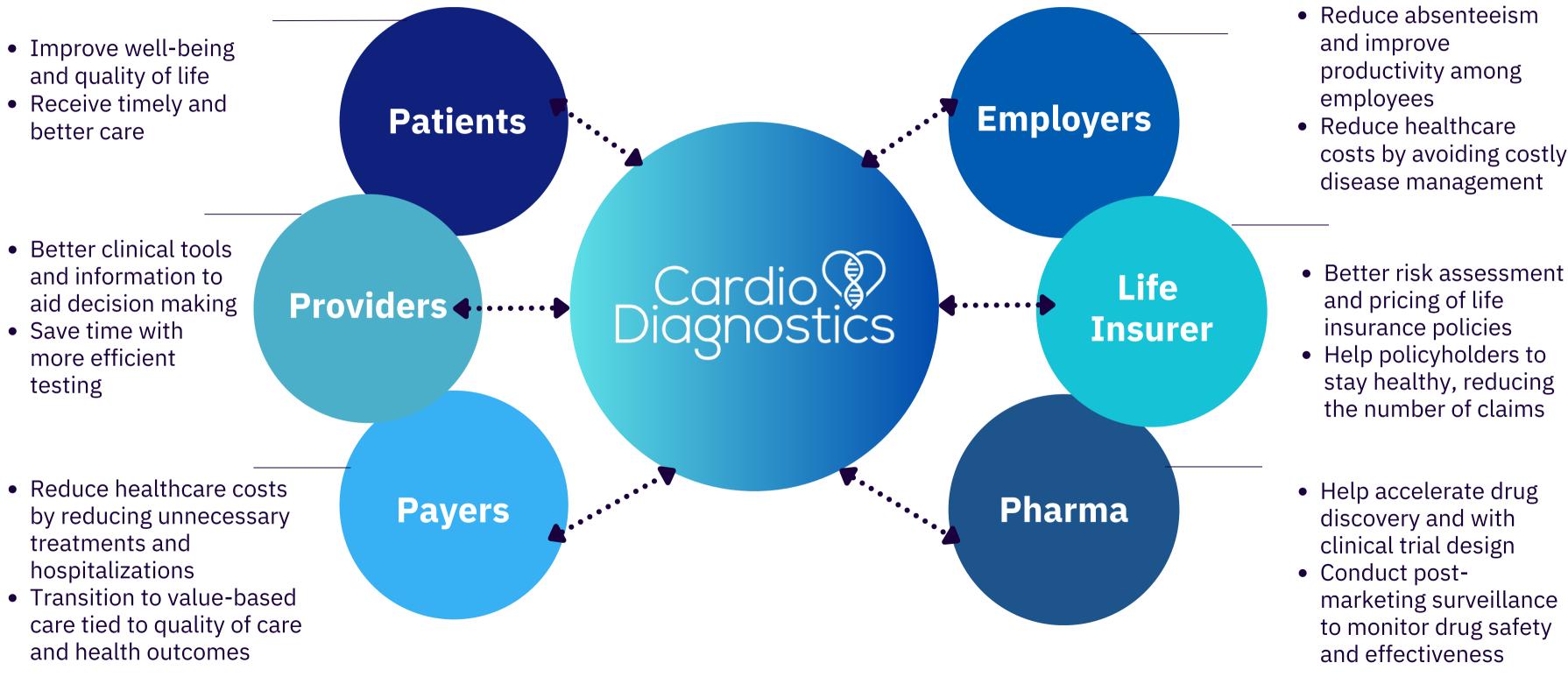


PrecisionCHD™



CardioInnovate360™

Our Differentiated Solutions Address the Needs of Major Healthcare Stakeholders



- Better risk assessment and pricing of life insurance policies
- Help policyholders to stay healthy, reducing the number of claims

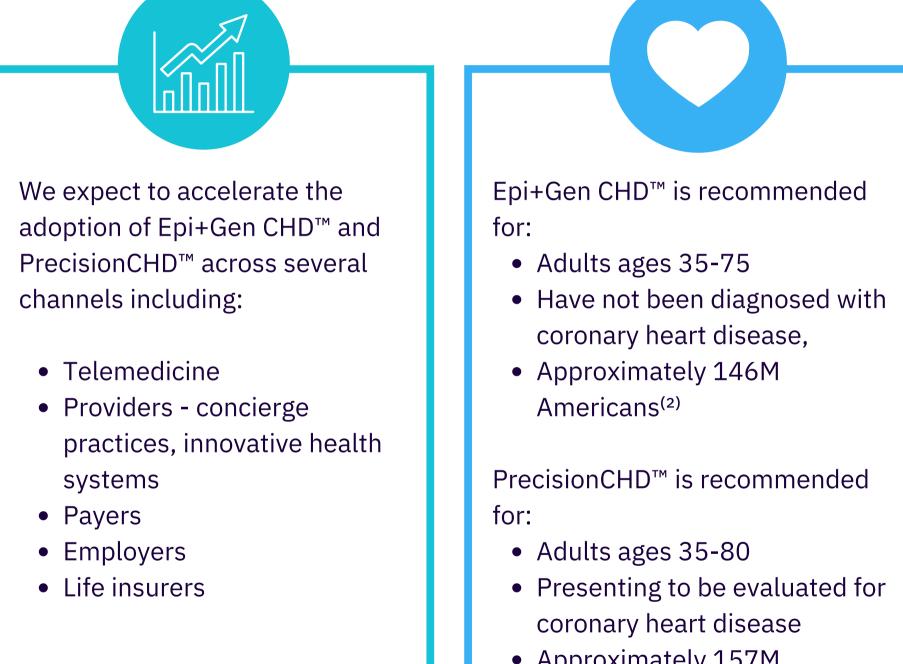
Clear, Key Differentiations for Coronary Heart Disease

	Cardio (P) Diagnostics	Hospitals & Clinics	23andMe∘		A ALIVECOR®	somalogic	cleerly
SENSITIVE EPIGENETICS BASED TEST			X				
CORONARY HEART DISEASE SPECIFIC			×		X	×	
PHYSICIAN ORDERED AND/OR INTERPRETED			X			×	
AT-HOME TESTING AVAILABLE							
MULTIPLE DNA BIOMARKERS-BASED TEST		X		×	X	X	×
MONITOR TREATMENT RESPONSE (1)		(2)		×			X

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⁽¹⁾ Comparison to PrecisionCHD for CHD detection ⁽²⁾ Comparison to detection tests such as exercise ECG

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

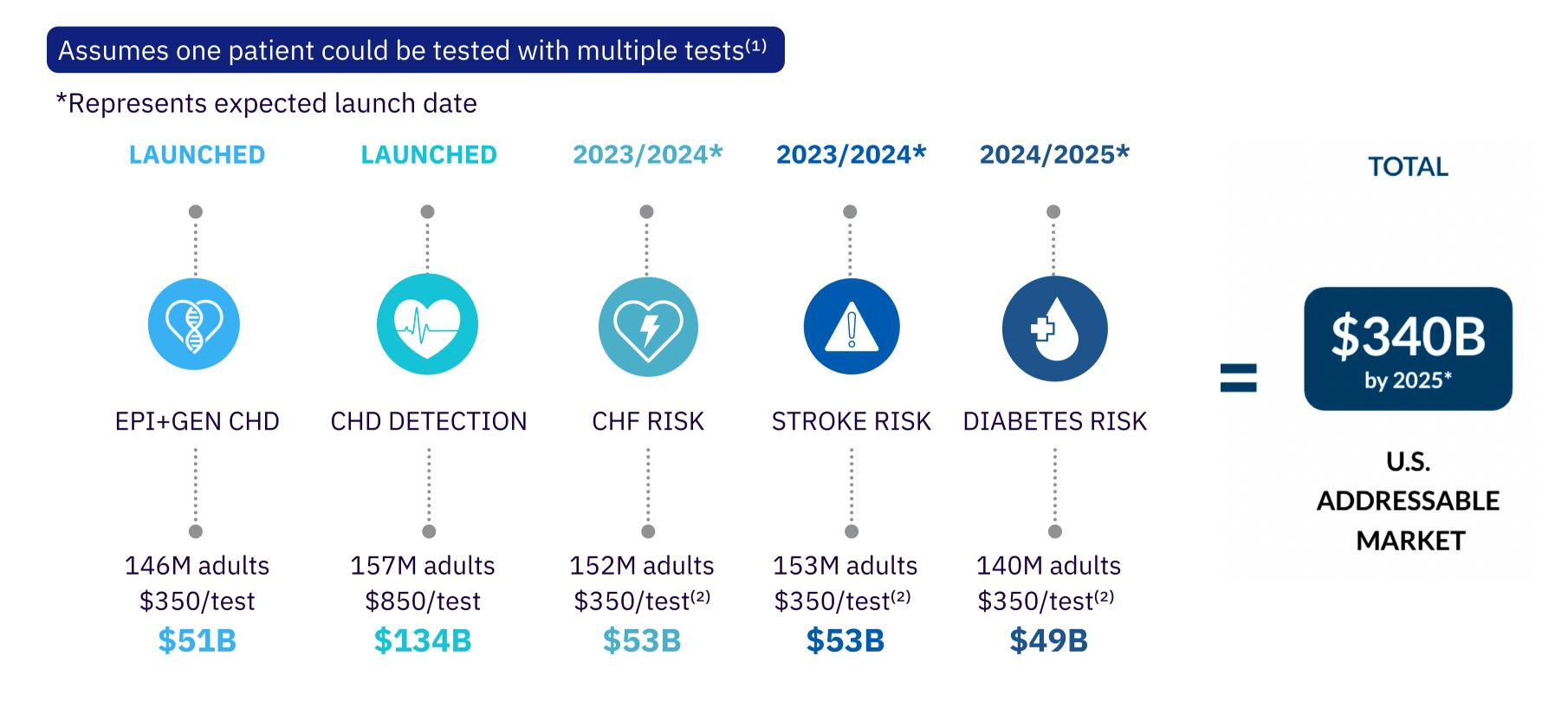


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We intend to accelerate the adoption of both tests by:

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

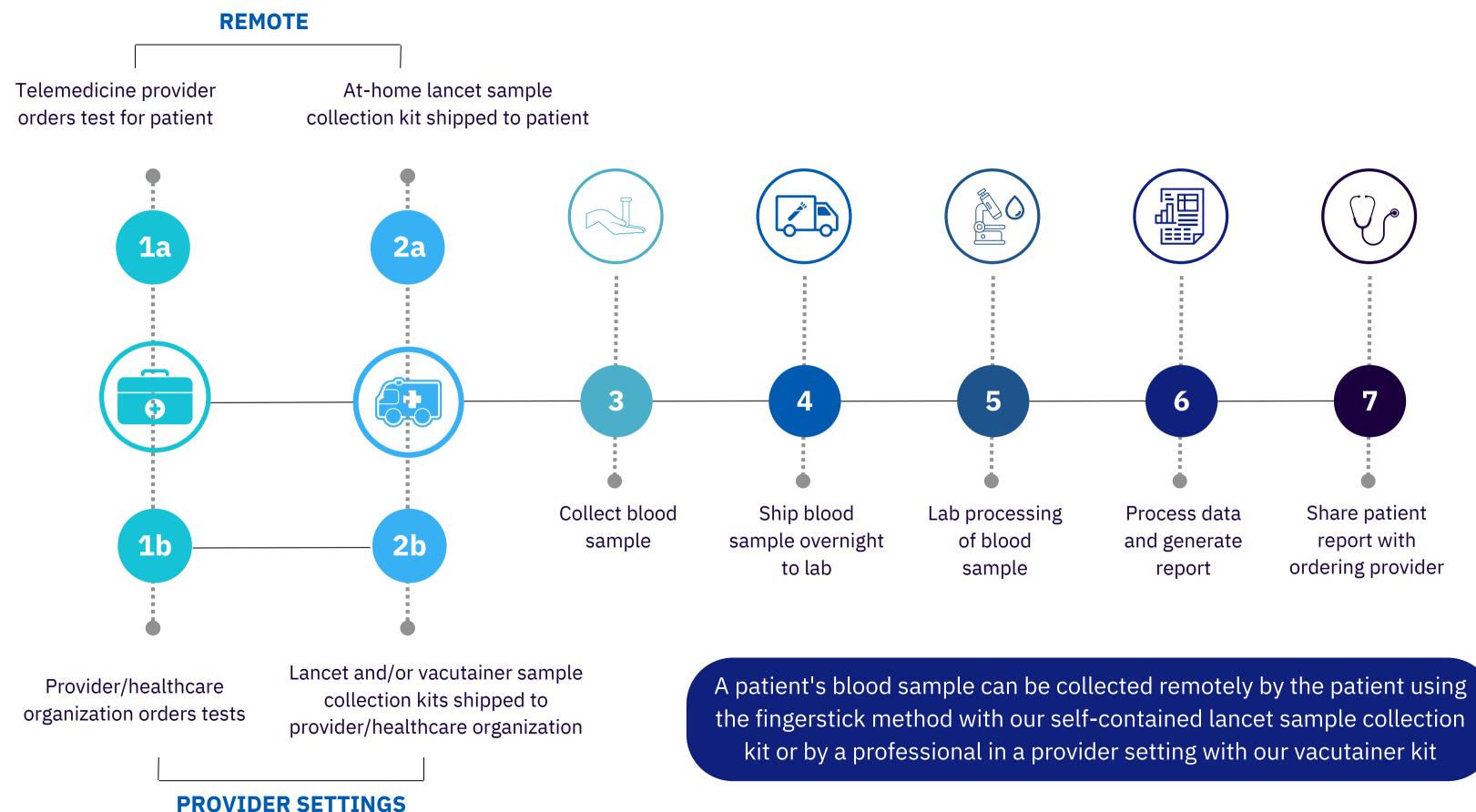
The Integrated Genetic-Epigenetic Engine[™] Can be Leveraged Repeatedly



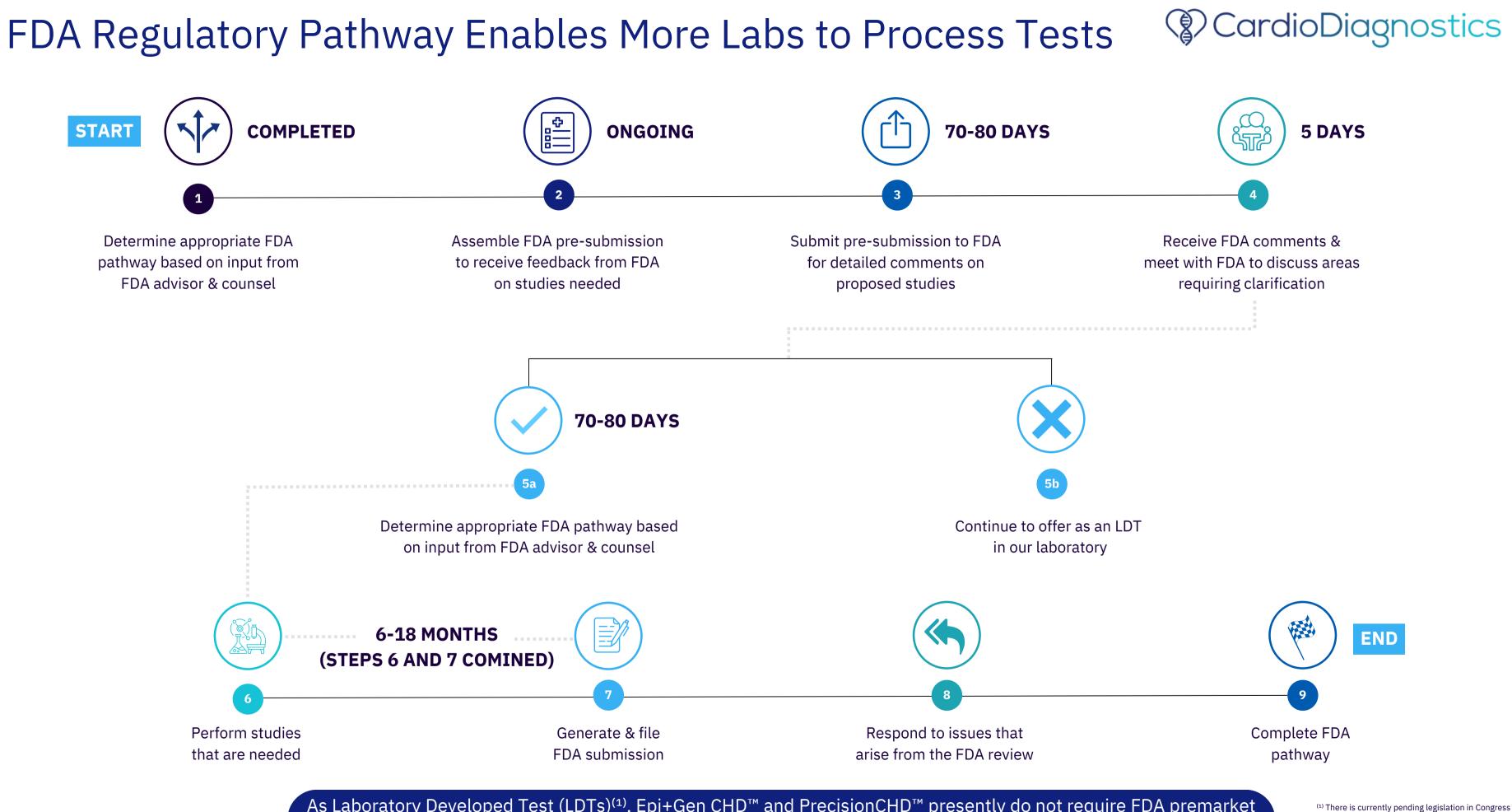


Source: Cardio Diagnostics estimate for US market based on 2020 US Census datas ⁽¹⁾ Assumes each test is administered to each patient a single time in a year although some patients may be eligible to be re-tested in less than a year ⁽²⁾ Assumed price per test

A Scalable Testing & Reporting Process to Fulfill Increasing Demand







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.

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.

Pursuing A New Standard of Care for Cardiovascular Medicine





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⁽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

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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 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

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Elisa Luqman, JD MBA

CFO

Team Continued



Tim Dogan, PhD

СТО

12+ years in high performance computing systems Co-inventor of the Integrated Genetic-Epigenetic Engine[™] PhD in Mechanical Engineering from the University of Iowa 13+ years in commercializing complex technologies and solutions Growth architect at GreenLight Medical/Symplr, Lumere/GHX JD from the University of Minnesota

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Khullani Abdullahi, JD

VP of Revenue & Strategy

Achieved and Upcoming Milestones

Completed Q1 2023 milestones

- Partnerships with concierge and executive practices, Healing Sanctuary and Houston Concierge Medicine
- Launch of second test, PrecisionCHD[™], for the detection of coronary heart disease
- Notice of allowance of patent in China
- 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

• Completed Q2 2023 (as of 05/12/2023) milestone

- Strategic engagement with Lifespan.io to drive longevity and heart disease research and education
- 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

• Expected 2023 (05/13/2023 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

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HOUSTON CONCIERGE MEDICINE

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INTROUCING

PrecisionCHD[™]

For Early Detection of Coronary Heart Diseas

Revolutionizing Cardiovascular Medicine With Epigenetics, Genetics, & Artificial Intelliger

Cardio Diagnostics

PRESS RELEASE

the VP of Clinical Innovation at Mercy Technology Services, the ical support arm of Mercy Healthcare, has joined Card nostics as a strategic advise



STRATEGIC ADVISOR









Partnering to make available regular on-site heart attack prevention fairs for selfinsured employers throughout Oklahoma, Arkansas, Missouri, and Kansas



CardioDiagnostics

JUST ANNOUNCED

China's Patent Office has issued a Notice of ance to the University of Iowa Research on, exclusively licensed to Cardio Diagnostics Inc.'s founders from UIRF for Chinese Patent Application

No. 201780049286.4

ed "Compositions and Methods for Detectin sition to Cardiovascular Disease

Announcing the availability of

CardioInnovate360™

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 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.

For more information, please email:



investors@cardiodiagnosticsinc.com





Cardio (\$) Diagnostics

Revolutionizing Cardiovascular Medicine With Epigenetics & AI

APPENDIX

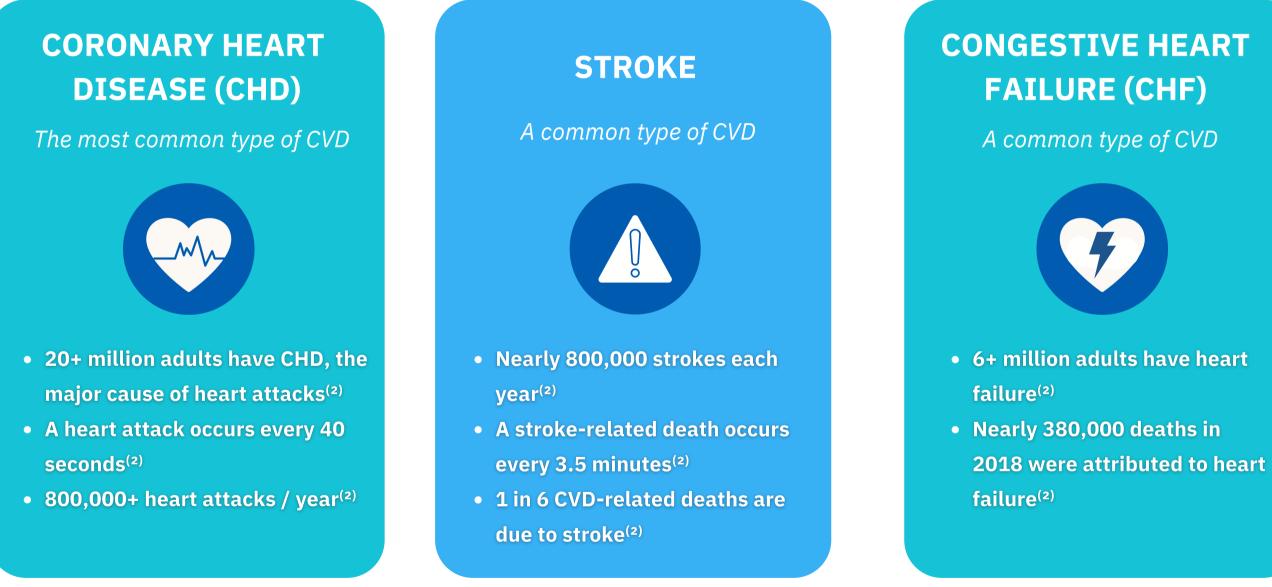
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Revolutionizing Cardiovascular Medicine With Epigenetics and AI



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⁾



(2) CardioDiagnostics

DIABETES

A major risk factor for CVD



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

⁽¹⁾ CDC Foundation ⁽²⁾ American Heart Association ¹⁾ Johns Hopkins Medicine

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**





Epi+Gen CHD

3-Year Coronary Heart Disease Risk Assessment

(1) This means that for every 100 men and 100 women deemed "at-risk" for a CHD event, the test correctly identifies 76 men & ⁽²⁾ FRS: Framingham Risk Score, PCE: ASCVD Pooled Cohort Equation Dogan et al., 2021, Epigenomics ⁴⁾ Jung et al., 2021, Epigenomics

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

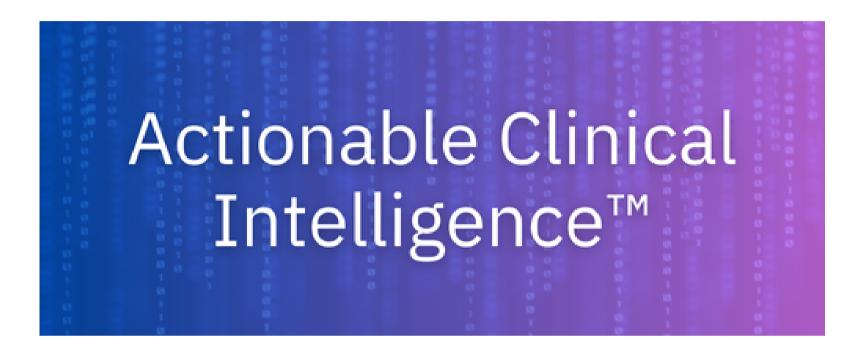


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⁽¹⁾ This means that for every 100 men and 100 women deemed "have" CHD, the test correctly identifies 80 men & 76 women ⁽²⁾ Philibert R et al., 2023, In Submission ⁽³⁾ Morrow D et al., 2018, A Textbook of Cardiovascular Medicine

Actionable Clinical Intelligence[™]: Assisting Clinicians in **Personalizing Clinical Decision Making**

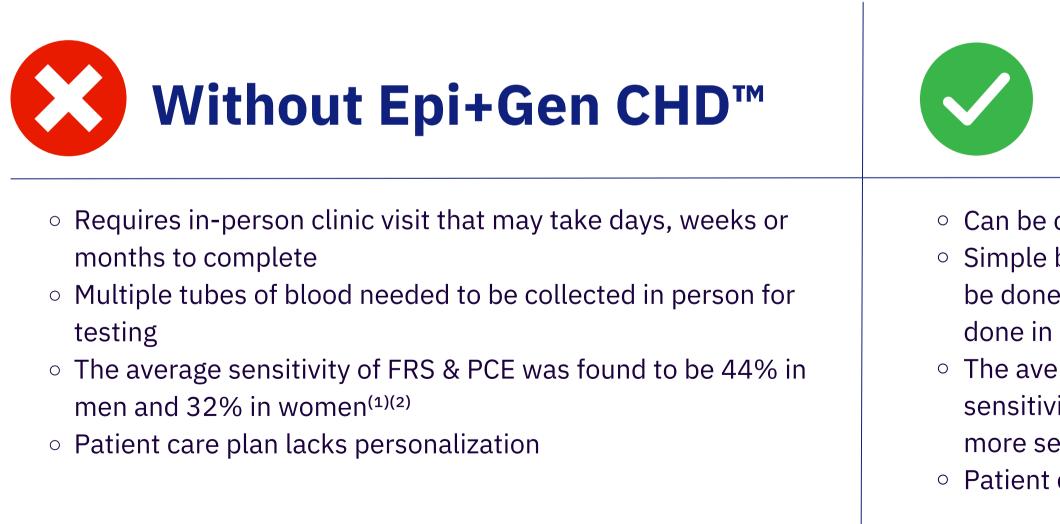


- A **one-of-a-kind platform** that offers new epigenetic and genetic insights to clinicians prescribing the Epi+Gen CHD[™] and PrecisionCHD[™] tests. These insights are:
 - Generated by integrating the test results with a patient's unique epigenetic and genetic biomarkers together with clinical information 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



CardioDiagnostics

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



- 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⁾

- - 45-68%⁽²⁾





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

CardioInnovate360[™]: A BioPharma Research System That Harnessess 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
 - $\circ~$ Additional health economic studies are ongoing

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Epigenomics

Research Article

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

eshanthini V Dogan^{*.1,2}, Stacey Knight^{3,5}, Timur K Dogan¹, Kirk U Knowlton³

Cardio Disposici Y Imidea Y. Conshile, IA 52241, USA Dispatiment of Biomedical Engineering, University of Xinea, Iona City, IA 52242, USA "Internovatina Heat Instatus, Internovatina Healthcare, Sait Lake City, UT 84103, US "Dispatiment of Psychiatry, Liversity of Xinea, Iona City, IA 52242, USA "Dispatiment of Medicine, Liversity of Xinea, Solara City, XI 84102, USA

Vim: The Framingham Risk Score (FRS) and ASCVD Pooled Cohort Equation (PCE) for predicting risk for ncident coronary heart disease (CHD) work poorly. To improve risk stratification for CHD, we develpeed a novel integrated genetic-epigenetic tool. Materials & methods: Using machine learning techsiques and datasets from the Framingham Heart Study (FRS) and Intermountain Healthcare (IM), we developed and validated an integrated genetic-epigenetic model for predicting 3year incident CHD. Reults: Our approach was more sensitive than FRS and PCE and had high generalizability across cohorts: t performed with sensitivity/specificity of 79/75% in the FHS test set and 75/72% in the IM set. The entitivity/specificity was 15/39% in FHS and 31/89% in IM for FRS, and sensitivity/specificity was 17/3% n FHS and 69/55% in IM for PCE. Conclusion: The use of our tool in a clinical setting could better identify anients at high risk for a heart tatak.

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

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

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

Zoronary heart disease (CHD) is the most common type of heart disease and was responsible for over 360,000 lachs in the USA in 2017 [1]. In order to decrease this recurring toll, a number of primary prevention risk estimators ave 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 sy optentially treatable parameters, such as serum lipid levels, howns to be associated with risk for CHD [2,3]. Septier the magnitude of these efforts, current risk scores often lack in sensitivity and specificity. As a result, there is a need for alternative primary revention 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 $i+\tau_{\rm T}$. 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

Younsoo Jung¹, David Frisvold², Timur Dogan¹, Meeshanthini Dogan¹ & Rob Philibert^{*,1,3} 'Cardio Diagnostics Inc., CoraWile, IA 52241, USA "Denotement of Recognicity Linguistical Genes Insue City IA 53242, USA

³Department of Psychiatry, University of Iowa, Iowa City, IA 52242, U

Author for correspondence: robert-philibert@uowa.edu Aim: New epigenetically based methods for assessing ris

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 re-CHD⁻¹ test with those of existing tests using a cohont Markow simulation model. **Results:** use of the new test was associated with both better survival and highly competitive negati cost-effectiveness ratios ranging from -842.000 to -83000 per quality-adjusted life year f and without a secondary test. **Conclusion:** The new integrated genetic/epigenetic test wal lives under most real-world scenarios.

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 • epigi medicine

The spitaling cost of healthcare has increased the need for better prevention strategies for cost lineses such as diabetes and heart disease. In particular, there have been represted calls for be for use in preventative interventions (1),2). Prior to the completion of the human genome sequenmajority of the biomarker discovery efforts employed metabolomic or proteomic methods to ide markers (1). Since then, scientists have complemented these califer approaches by incorporating is genotyping methods to idefunify genetic variations predictive of disease onset and severity (6). De pointie of these nucleic acid technologies, he impact of genetic approaches for identifying clinic biomarkers predictive of risk for illnesses such as heart disease has been limited (3). Instead, due to to cost-to-information content ratio of the genetic-based approaches, clinicians continue to rely on proteomic-based approaches for assessing risk of onset of syndromes, such as coronary heart disease whose management constitutes the bulk of dy-to-dy-clinical interactions for primary care practin

Recent advances in epigenetics have opened yet another frontier for developing clinical biol in assessing the risk or presence of common syndromes. In particular, the US FDA's 2014 approval 1 acts that uses a combination of genetic, epigenetic and proteomic tests to assess the presence of colonhas alerted both clinicians and healthcare payers to the potential of epigenetic testing technologies 17. TI

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 opigenetically based test will not be the last: Taryma-Lesniak *et al.* tecently reviewed the landscape of *in vitro* diagnostic tests and found 25 tests f

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 commer

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 Meesha Dogan, Willem Phillbert, Younsoo Jung, Tim Dogan, David Frisvold, Allan Andersen, Eric Hoffman and Robert Phillbert originally published 8 Nov 2021 [https://doi.org/10.1161/circ.144.suppl_1.13530] Circulation.2021;144:A13530

 Footnotes
 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

Supply Chain & Laboratory Strategy

SAMPLE COLLECTION KIT CONTENTS & ASSEMBLY

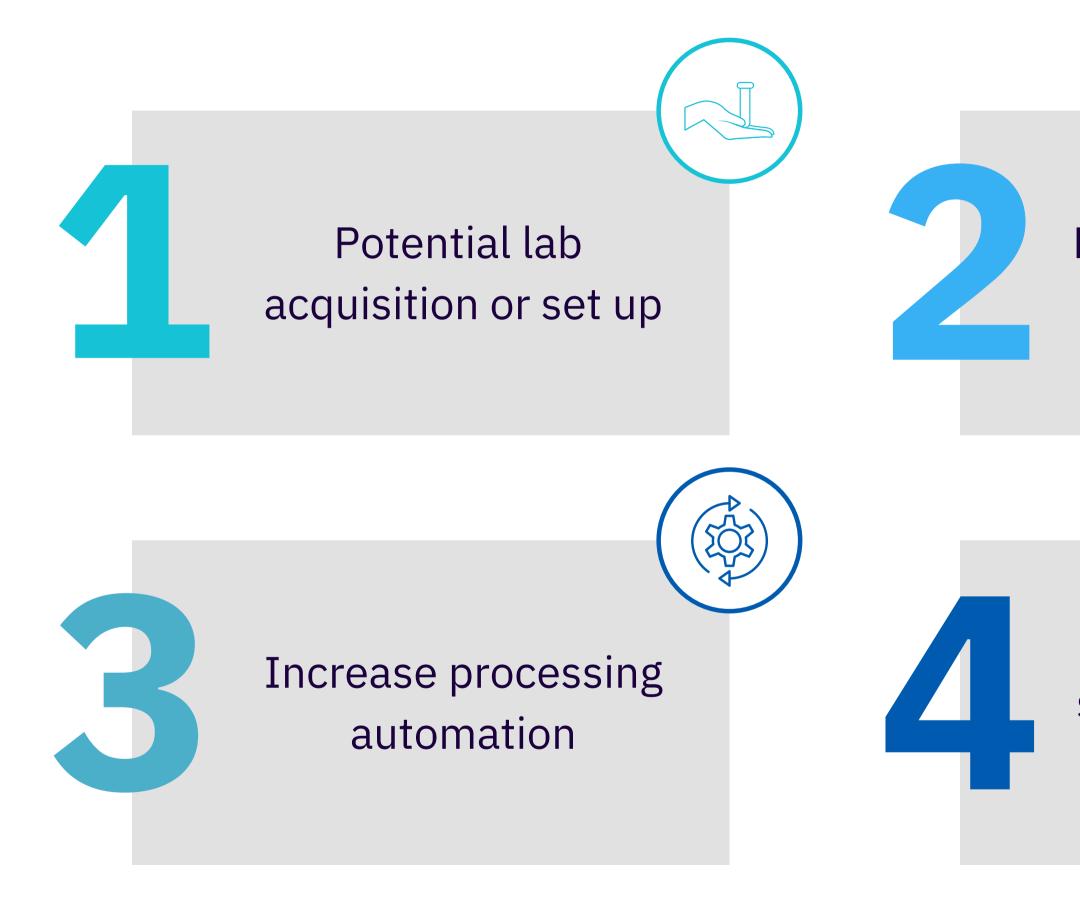
- Common kit contents that can be sourced from multiple distributors
- Identified multiple distributors to diversify supply chain
- Most kit contents are shelf-stable for years and can be sourced well in advance
- Maintain inventory of fully assembled kits to meet six months of expected demand
- Assembly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

- 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

CardioDiagnostics

LABORATORY STRATEGY

Gross Margin Expansion Opportunity







Process larger sample batches



Bulk shipping of sample collection kits and/or samples

Product and Company Recognitions



nature research awards Winner Biotech Innovation Showcase Award 2019



IOWA BIOTECH SHOWCASE & CONFERENCE









Disruptive Technology Award Semifinalist ⁽¹⁾

⁽¹⁾ Finalists to be announced around May 24, 2023