StageZero Life Sciences, Ltd
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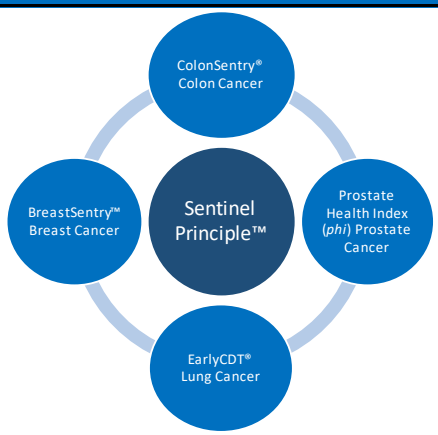
Ticker (Exchange)	SZLS-TSX
Recent Price (04/08/2020)	$0.06
52-week Range	$0.03 – 0.20
Shares Outstanding	288.7 M
Market Capitalization	$17.3 M
Average 10-day volume	1,271,379
Insider Ownership +>5%	5%
Institutional Ownership	NA
EPS (Year ended 09/30/19)	$0.01
Employees	19

SZLS (TSX) One-year Stock Chart

STAGEZERO PRODUCT PORTFOLIO



COMPANY DESCRIPTION

StageZero Life Sciences, Ltd ("StageZero" or "the Company") is a revenue-generating innovator in the **liquid biopsy†** space, dedicated to the early detection of cancer and multiple disease states. The Company is focused on developing and commercializing proprietary blood-based diagnostic solutions to aid in the detection of cancer at the earliest possible stage. StageZero's proprietary Sentinel Principle® technology platform is a liquid biopsy technology that uses a blood sample to detect cancer and other disease. The technology is based on the scientific observation that circulating blood reflects, in a detectable way, what is occurring throughout the body. Thus, by conducting a minimally invasive blood draw, the Company can analyze the blood sample to detect disease-specific **biomarkers** that signal the possible presence of cancer. The science behind the Sentinel Principle® has led to the development of the Company's flagship product, ColonSentry®, a blood-based test for assessing an individual's risk for colorectal cancer (CRC). StageZero also offers diagnostics and risk stratification tests to assess the probability of having four of the most prevalent cancers: CRC, lung (*Early*CDT®-Lung), prostate (Prostate Health Index [*phi*]), and breast cancers (BreastSentry™). StageZero is using its Sentinel Principle® technology to develop its next generation test, Aristotle™, expected to launch in 2021. Aristotle™ is a multi-cancer panel for the simultaneous screening of 10 cancers (CRC, prostate, cervical, endometrial, breast, ovarian, liver, bladder, nasopharyngeal, and stomach cancer) from a single blood sample. The Company's commercialization strategy aims to shorten the lengthy market-entry process of new diagnostic tests, targeting four market segments: (1) physician practices; (2) **telehealth**–consumer directed; (3) large healthcare systems; and (4) large employers/high risk populations.

KEY POINTS

- Initially developed from a clinical study involving approximately 10,000 subjects, ColonSentry® was commercialized in 2014 and has been successfully used in over 100,000 patients in the U.S.
- In March 2019, StageZero launched its first nationwide telehealth initiative, making its *phi* test available for online purchase through its portal mycancerrisk.com. The Company has begun to process initial patient orders.
- The Company has experienced early success with a Midwest hospital system and initiated a contract with a large healthcare system to offer its array of cancer screening tools.
- In the large employer/high risk market, StageZero began screening firefighter groups and has engaged another large employer (with over 100,000 employees) to use its products.
- The Company further operates a **CAP**-accredited and **CLIA**-certified reference laboratory based in Richmond, Virginia.
- StageZero's long term goals are to achieve profitability (expected in 2020) and to launch the Aristotle™ test (expected in 2021).
- As of September 30, 2019, StageZero had $411,445 in cash and cash equivalents.

All amounts in U.S. dollars unless stated otherwise.

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All amounts in U.S. dollars unless stated otherwise.

Executive Overview

StageZero Life Sciences, Ltd ("StageZero" or "the Company") is a revenue-generating innovator in the liquid biopsy space dedicated to the early detection of cancer and multiple disease states. The Company is focused on developing and commercializing proprietary blood-based diagnostic solutions that reduce the incidence of late stage cancer and aid in the detection of cancer at the earliest possible stage.

StageZero's proprietary Sentinel Principle® technology platform is a liquid biopsy technology that uses a blood sample to detect cancer in early stages. The technology is based on the scientific observation that circulating blood reflects, in a detectable way, what is occurring throughout the body. As blood circulates, communication occurs between cells in blood and tissue. As a result, different clinical conditions generate specific and detectable changes in **gene expression** in blood cells. Thus, by conducting a minimally invasive blood draw, the Company can analyze the blood sample to detect disease-specific biomarkers that signal the possible presence of cancer.

The science behind the Sentinel Principle® has led to the development of the Company's flagship product, ColonSentry®, a blood-based test for assessing an individual's risk of having colorectal cancer (CRC). StageZero also offers early cancer diagnostics and **risk stratification** tests used to assess the probability of having four of the most prevalent cancers: CRC, lung (*Early*CDT®-Lung), prostate (Prostate Health Index [*phi*]), and breast cancer (BreastSentry™), as summarized in Figure 1.

Figure 1

STAGEZERO'S PRODUCT PORTFOLIO

Blood-based Cancer Detecting Biomarker Tests	
ColonSentry® - Colorectal Cancer	Prostate Health Index - Prostate Cancer*
EarlyCDT® - Lung Cancer*	BreastSentry™ - Breast Cancer*

** licensed from third parties*

Sources: StageZero Life Sciences, Ltd. and Crystal Research Associates.

StageZero is further utilizing its Sentinel Principle® technology to develop its next generation test, Aristotle™, expected to launch in 2021. Aristotle™ is a multi-cancer panel for the simultaneous screening of 10 cancers (CRC, prostate, cervical, endometrial, breast, ovarian, liver, bladder, nasopharyngeal, and stomach cancer) from a single sample of blood. The Company is moreover planning to expand the applications of Aristotle™ beyond oncology to help in the diagnosis of diseases in gastroenterology, neurology, cardiology, and autoimmune disorders. In addition to building a pipeline of products for early cancer detection, the Company operates a CAP-accredited and CLIA-certified reference laboratory based in Richmond, Virginia, which conducts sample processing for the ColonSentry® test as well as for the licensed biomarker tests for breast and prostate cancers.

Cancer Diagnostics

In 2020, more than 1.8 million new cancer cases are expected to be diagnosed in the U.S. and 606,520 deaths, representing the second most common cause of death in the U.S. (Source: American Cancer Society's *Cancer Facts & Figures 2020*). Early detection of cancer has been proven to improve survival rates and quality of life, decrease the cost of treatment, and reduce the complexity of the therapeutic regimen. Despite this, a high number of cancers are detected in advance stages, with 40% of screenable cancers diagnosed late. This is due to the fact that, despite the availability of cancer screening tests, patients are not adhering to preventive screening guidelines. For example, among the populations suggested for screening, only two-thirds are up-to date with CRC screening guidelines, only 35.8% reported having a **Prostate Specific Antigen (PSA)** test in the past year, and only 3.9% of high-risk smokers in the U.S. received their recommended **low dose computed tomography (LDCT)** lung cancer screening (Sources: *Preventing Chronic Diseases´*Volume 15 (E97), 2018, and *JAMA Oncology*, Vol. 3(9):1278-1281, 2017).

StageZero's Products

Stage Zero is focused on developing and commercializing proprietary molecular diagnostic tests for the early detection of diseases and for personalized health management, with a primary focus on cancer-related indications.

ColonSentry®

ColonSentry® is a proprietary blood-based risk prediction test that uses a seven-gene biomarker panel to stratify patients into subgroups according to their current risk, or probability, of having CRC—the third most frequently diagnosed cancer in men and women in the U.S. Unlike other "yes or no" screening tests, ColonSentry® provides an actual risk score for a patient. If the ColonSentry® score is elevated, indicating an increased probability of CRC, patients are encouraged to have a **colonoscopy**. Initially developed in 2008 from a clinical study involving approximately 10,000 subjects in North America, ColonSentry® was broadly commercialized in 2014 and has been used successfully in over 100,000 patients throughout the U.S.

The predictive ability of the ColonSentry® can help detect CRC in its earliest stages, leading to a better prognosis. CRC diagnosed in its localized stage display a 90% **5-year survival**, as opposed to only a 14% 5-year survival rate of patients with late stage disease (Sources: *CA: a Cancer Journal for Clinicians* and Cancer.org). The test has been validated by multiple clinical trials, including a key study of 10,000 patients in North America. According to the Company, ColonSentry® has demonstrated a **negative predictive value** (the probability that subjects with a negative screening test do not have the disease) of 99.6%, which means that the chances of missing colorectal cancer is less than 0.4 percent (Soure: *International Journal of Cancer*, 126:1177-1186,2009).

ColonSentry® is a patient-friendly, blood-based test that can be easily incorporated into a patient's routine annual exam, providing significant clinical advantages, including (1) increases patients CRC screening compliance, with patients two-times more likely to comply with a **colonoscopy** following an elevated ColonSentry® score; (2) increases the effectiveness of current screening methods, with colonoscopies detecting 2.1 to 4.7 times more CRC lesions following a ColonSentry® test; and (3) provides financial benefits to both the consumer and healthcare plans, with ColonSentry® reducing healthcare costs by more than 20% through early intervention.

Prostate Health Index (phi)

The Prostate Health Index (*phi*) is a convenient blood test that uses three different PSA biomarkers (PSA, **free PSA**, and **pro2 PSA**) as part of a sophisticated algorithm to more reliably determine the probability of prostate cancer in patients with elevated PSA levels. *Phi* helps physicians distinguish prostate cancer—the most common cancer among men—from benign conditions. The *phi* test is three times more specific in detecting prostate cancer than the PSA test and has been found to reduce unnecessary biopsies by 30% percent (Source: Mayo Clinic). Early detection of prostate cancer is key, with five-year survival for prostate-cancer patients at nearly 100% for early stage disease and decreasing to 31% if the cancer is detected at a later stage (Source: American Cancer Society's *Cancer Facts & Figures 2020*).

Developed by Beckman Coulter and widely used in Europe under CE mark approval, the *phi* index was granted approval by the U.S. Food and Drug Administration (FDA) in June 2012. The Company executed an agreement with Beckman Coulter in 2014 that allows it to include the *phi* test in its portfolio of cancer screening offerings. The *phi* test is currently available and is the centerpiece of the Company's telehealth initiative.

EarlyCDT®-Lung

*Early*CDT®-Lung is a sophisticated blood test that, in combination with low dose computed tomography (LDCT), aids physicians in the early detection of lung cancer, the leading cause of cancer death among adults in the U.S. *Early*CDT®-Lung measures a panel of seven **autoantibodies** associated with lung cancers and can detect all types of lung cancer at all stages of disease with high accuracy. StageZero licensed *Early*CDT®-Lung in January 2014 from Oncimmune Ltd, a UK-based company, for marketing, sale, and distribution of this test throughout the U.S.

*Early*CDT®-Lung is an **enzyme-linked immunosorbent assay (ELISA)** that measures the blood levels of seven lung cancer associated autoantibodies. Elevation of any one of the seven autoantibodies above a predetermined cut-off value suggests that a tumor may be present, necessitating a follow-up test. *Early*CDT®-Lung can help aid early lung cancer detection, leading to earlier intervention and better patient outcomes. In a cohort of 296 patients, a positive *Early*CDT®-Lung test was associated with a more than two-fold increase in the risk of lung cancer for nodules 4 to 20 mm (Source: *Journal of Thoracic Oncology*, Vol. 12(3):578-584, 2017).

BreastSentry™

In October 2014, StageZero in-licensed two blood-based biomarker **assays** (developed by sphingotec GmbH)—**proneurotensin (pro-NT)** and **proenkephalin (pro-ENK)**—which are highly predictive of a woman's risk for developing breast cancer. The Company used those two assays for the creation of BreastSentry™, a blood test and algorithm intended to aid physicians in identifying women who are at risk for developing breast cancer, the most frequently diagnosed cancer and the second leading cause of cancer death among women in the U.S. (Source: *CA: a Cancer Journal for Clinicians*, Cancer Statistics 2019). The BreastSentry™ test provides patients with their risk of developing breast cancer in the future. Based on a patient's risk score, physicians may monitor patients more closely or prescribe additional screening.

Over a third of breast cancer cases are diagnosed in the advance stages of the disease, mainly due to the shortcomings of mammograms. An estimated 20% of breast cancers are missed at least once by mammography. In addition, mammograms result in a high number of false positives, with approximately half of the women over a 10-year period expected to have a **false-positive** (Source: American Cancer Society). Five-year survival for breast cancer patients with early stage disease is 99%, and survival rates remain high at 10 years. However, that figure decreases to 27% for late stage cancers (Source: American Cancer Society's *Cancer Facts & Figures 2020*).

Aristotle™

Utilizing its Sentinel Principle® technology, StageZero is developing Aristotle™, its next generation test. Aristotle™ is a multi-cancer panel for the simultaneous screening of 10 cancers (colorectal, prostate, cervical, endometrial, breast, ovarian, liver, bladder, nasopharyngeal, and stomach cancer) from a single sample of blood. The Company has conducted early validation studies for the technology and anticipates a 2021 market launch. StageZero is using Aristotle'™s capabilities to develop gender-specific cancer detection panels. The Company is developing the first multi-cancer detection panel for women, aimed at detecting the most prevalent cancers affecting women: breast, lung, colon, cervical, thyroid, uterus, stomach, ovarian, liver, and Non-Hodgkin lymphoma. A multi-cancer detection panel for men, for the diagnosis of prostate, liver, bladder, nasopharyngeal, colorectal, and stomach cancer, is in development. Furthermore, the Company is planning to capitalize on the flexibility of its Sentinel Principle® technology platform and expand the applications of Aristotle™ beyond oncology, to help in the diagnosis of disease states in gastroenterology, neurology, cardiology, autoimmune disease, heart disease, and psychiatric disorders.

Commercial Activities

The typical path to commercialize new, novel diagnostics is often lengthy, mainly due to medical billing companies long initiation cycle and uncertainty of their acceptance, reimbursement amount, and payment timeframe for new tests. The Company is implementing a commercialization plan that aims to shorten this cycle, intended to drive adoption and increase utilization of its tests. Supported by its Company-wide efforts and strategic alliances, StageZero has targeted four key medical market segments that would accelerate and advance the uptake and adoption of the Company's proprietary cancer tests: (1) small clinical and physician practices; (2) telemedicine–consumer directed; (3) large healthcare systems; and (4) large employers/high risk populations.

Physicians Practices

The Company is steadily expanding its physician's network, with reimbursement for the tests coming from billing to insurers and patient-pay. This sector includes StageZero's efforts to target **concierge physicians** and executive health/wellness programs, whose practice models are more likely to attract patients who want to be proactive about their health. As such, growth of the Company's physician practice network supports StageZero's patient-directed testing model in the form of its telehealth program. The Company expects the physician practice segment to contribute about 10% of its test volume.

Telehealth—Patient-Directed

StageZero has been building out its capability in telehealth required to support a patient-directed testing model. This includes developing a system by which patients can request the tests, pay for them, and receive the results; recruitment of over 200 physician networks who are expected to facilitate and authorize diagnostic testing and provide guidance with test results; a national blood draw network that includes more than 10,000 draw sites and mobile phlebotomists; and a marketing campaign to raise awareness of its products.

A key initiative to support the Company's telehealth efforts is the development of MyCancerRisk™, an online portal where patients can get information about the Company's products and/or purchase and initiate testing. The portal allows patients to pay one flat fee for the test, the physician consult, and blood draw services. On March 2019, StageZero launched the first of several initiatives to make patient-directed testing available nationwide. The first tests available for online purchase are the ColonSentry® and *phi* tests.

Healthcare Plans and Systems

The Company considers large healthcare systems, a network of multiple hospitals and several thousand physicians normally owned by a healthcare plan, as one of its largest opportunities. This stems from two facts: the large number of patients each system can provide, as well as a flat fee per test (invoiced and paid within 45 days). However, implementation of Company programs on these massive organizations is complex, with a sales cycle of over two years. StageZero is relying on its Company-wide efforts, as well as strategic alliances, to secure multi-year agreements with a large healthcare system to administer the Company's risk assessment tests. As a result of these efforts, StageZero initiated a contract with a large healthcare system to improve patient compliance with cancer screening (noting that the details of this contract are confidential).

Large Employers – High Risk Populations

Early detection of cancer as well as risk stratification is of critical importance to workers exposed to carcinogens. As part of its strategy to focus on larger opportunities that can create high volumes of tests, StageZero is targeting self-funded and large employer healthcare plans with companies that operate in high-risk environments who have a higher prevalence of cancer. The type of employers targeted by the Company include firefighters, oil and gas, coal and chemical plants, pilots and flight attendants, drivers, the military, as well as individual States who have specific populations they need screened. The Company currently offers large employers its full panel (colorectal, lung, prostate, and breast cancer tests), and it invoices a flat fee on a monthly basis. Reimbursement to the Company is direct and either immediate, or within 45 days upon invoice. StageZero is currently working with multiple high-risk

employee partners across the country and is in discussion with several other self-funded employer plans that have significant interest in the Company's programs.

As part of this initiative, StageZero began screening firefighter groups. Firefighters face a 9% increase in cancer diagnoses and a 14% increase in cancer-related deaths versus the average population, with cancer being the leading cause of line-of duty death among firefighters in the U.S., accounting for 61% of career firefighter deaths between 2002 and 2017 (Source: National Fire Protection Association [NFPA]). According to the Company, tests on two fire districts in 2018 reported cancer risks among firefighters far greater than the general population, with 41% and 34% of firefighters evaluated reporting elevated scores in each district, respectively.

Furthermore, the Company is expected to engage with large and mid-size employers to use its products. The target companies have many thousands of employees, a number of which work in high risk areas. The Company plans to start its programs in 2020 and expand with help from groups such as Mercer (a world leader in the health and benefits marketplace, delivering innovative solutions that address the health and wellness needs of organizations and their employees).

In order to support the sale of its products throughout these four channels, the Company has strengthened its salesforce through internal efforts as well as by implementing two key strategic partnerships: Coastal Medical, which will concentrate on increasing the outreach of the Company's products in Georgia and South Carolina (before expanding to other states), and Oncore Pharma, which aims to commercialize ColonSentry® in foreign markets other than the U.S. and Canada (with an initial focus on the Netherlands, Belgium, Luxemburg, Germany, France, Switzerland, Austria, Spain, Monaco, Italy, Portugal, United Kingdom, Ireland, Norway, Sweden, Finland, Denmark, Israel, and the United Arab Emirates). These partnerships are already providing results as seen by the October 2019 agreement between Oncore Pharma and BodyCheck NL for the distribution and sale of ColonSentry® throughout the Netherlands, Belgium, and Luxembourg (Benelux).

Company Information

Formerly known as GeneNews Ltd. (changing its name to StageZero Life Sciences Ltd on June 20, 2019), Stage Zero is headquartered in Richmond Hill, Ontario, Canada, and owns and operates a CAP-accredited and CLIA-certified reference laboratory based in Richmond, Virginia. The Company currently employs 19 individuals. On February 2020, the Company announced the closing of $1.85 million (CDN) in private placements to expand its commercial footprint in both the U.S. and abroad.

Company Leadership

Board of Directors

James R Howard-Tripp, Chairman and Chief Executive Officer (CEO)

Mr. Howard-Tripp has specialized in the research, development, and launch of innovative pharmaceutical products and the growth and development of the companies that research and market them. He has been involved in the management (GD Searle, Wyeth-Ayerst) and creation (Allelix, Labopharm, Dermacor) of several successful companies. He has 20 years of experience as a President and CEO and has sat on multiple boards of directors, on most as Chairman. As President and CEO of Labopharm (11 years), he oversaw the research, development, and approval of three products and the launch of two, with the lead product marketed in 19 countries and resulting in total end-user sales of approximately $100 million. During his leadership, Labopharm raised >$250 million in the public markets (US IPO $112 million in 2006) and earned >$100 million in deal revenue (partners Sanofi-Aventis, Purdue Pharma, Merck Inc., Grunenthal, Angelini, Esteve). Additionally, he has served on various scientific and industry committees as well as several not-for-profit boards.

Rory Riggs, Director

Mr. Riggs is CEO Locus Analytics LLC/Syntax LLC, as well as being the Managing Member of Balfour LLC, an investment management company. Since 1991, Mr. Riggs has been affiliated with ITIM Corp. and Pharmaceutical Partners LLC. He served as the President of Biomatrix, Inc. since April 1, 1996. He served as the Chief Financial Officer of Biomatrix from September 1996 to January 2000. From 1991 to 1994, he served as the Acting President and Chief Executive Officer of RF&P Corporation. Until 1990, he served as the Managing Director in the Mergers & Acquisitions Department at PaineWebber Incorporated, where he was employed for more than nine years. Mr. Riggs also served as an Associate at Strategic Planning Associates, the predecessor company to Mercer Management Consulting and has been involved in the start-up of many companies including: Chondrogene Limited, Cibus Genetics, Fibrogen, Inc., Royalty Pharma AG, Selectide Inc., Sugen Inc., eAppeals, LLC, Medrium, Inc., Pharmaceutical Partners, and Pacific Media. He was also involved in the founding or start-up of most of these companies. He co-founded RP Management, LLC in 1996 and has been its Chairman of the Board since 2003. He serves as the Chairman of the Board at Cibus Global, Ltd., eReceivables LLC, and Nucelis Inc. He served as the Chairman of GeneNews Limited from February 4, 2002 to July 2013 and has been its Director since 2000. He has been a Director at Intra-Cellular Therapies, Inc. since January 8, 2014. He has been a Non-Employee Director of FibroGen, Inc since October 1993. He serves as a Director of Cibus Global, Ltd. He serves as a Member of the Advisory Board at Celtic Pharma Management L.P. He served as a Director of Biomatrix, Inc. since October 1990. He served as a Director of Medrium, Inc. and Sparton Corp. Mr. Riggs received a B.A. Degree from Middlebury College and an MBA Degree from the Columbia University.

Harry Glorikian, Director

Since October 2014, Mr. Glorikian has served as an Entrepreneur In Residence to GE Ventures, and is currently a General Partner at New Ventures Funds (NV). Before joining NV Funds, he served as an Entrepreneur In Residence to GE Ventures – New Business Creation Group. He currently serves on the board of GeneNews Ltd. He also serves on the advisory board of Evidation Health (a digital health startup launched with support from GE Ventures), and several other companies. He is also a co-founder and an advisory board member of DrawBridge Health (a revolutionary diagnostics startup launched with support from GE Ventures). Mr. Glorikian holds an MBA from Boston University and a bachelor's degree from San Francisco State University. Mr. Glorikian has addressed the NIH, Molecular Medicine Tri-Conference, World Theranostics Congress, and other audiences, worldwide. He has authored numerous articles, appeared on CBS Evening News, and been quoted regularly by Dow Jones, The Boston Globe, Los Angeles Times, London Independent, Medical Device Daily, Science Magazine, Genetic Engineering News, and many other publications.

Garth MacRae, Director

Mr. MacRae has been a Director of Dundee Corporation, a merchant bank and financial services company, since 1991. Mr. MacRae is a chartered professional accountant, having received his designation in Manitoba in 1957, and has been a member of the Ontario Institute of Chartered Accountants since 1970. Mr. MacRae is also a director of a number of other public and private companies.

Milestones

During 2018, the Company's efforts centered around three key business-related activities that supported the long-term growth of StageZero's cancer test business: (1) the continued validation and commercialization of its cancer tests; (2) the creation of the infrastructure required to support a patient-directed testing model, including national provider networks and a blood draw network; and (3) the launch of a business development initiative to target larger healthcare systems and large employers. In 2019, the Company achieved significant milestones, as highlighted below, with additional potential milestones outlined thereafter.

Company Operation

- Officially changed its name from GeneNews Ltd. to StageZero Life Sciences Ltd, with the related change to ticker symbol (TSX: SZLS)
- Closed $5.2 million (CDN) in Private Placement offerings for 2019
- Expanded its commercial footprint in both the U.S. and abroad with key strategic partnerships:
    - Signed a global distribution contract with Oncore Pharma, which aims to deploy a total of 1,750,000 ColonSentry® tests over the next 5 years
    - Expanded its U.S. salesforce through a contract with Coastal Medical to increase outreach to physician practices and hospital systems throughout the Southeast

Physicians Practices Market

- Continued to expand the small clinical practice base and upgrade billing and revenue collection systems

Telehealth—Patient-Directed Market

- Initiated the patient-directed testing program with 8,000+ draw sites and TeleHealth Physician Networks
- Launched the Company's first telehealth program for marketing the Prostate Health Index (*phi*) directly to patients nationwide
- Launched a new online marketing initiative for prostate cancer awareness month to support the commercialization of its Prostate Health Index (*phi*)

Large Healthcare Plans and Healthcare Systems Market

- Initiated a contract with a large healthcare system to improve patient compliance with cancer screening; also initiated test implementation planning to run parallel with contract completion

Large Employers/High Risk Patient Population Market

- Consolidated planning with large employers of high-risk employees to initiate extensive screening programs
- Began screening firefighter groups and engaged another large employer (with over 100,000 employees) to use its products

Aristotle™

- Initiated full clinical validation of Aristotle™

Potential Milestones (2020)

StageZero's long term goals center around two key milestones: (1) generate revenue and achieve profitability during 2020; and (2) launch the Aristotle™ test during 2021. To accomplish these objectives, the Company expects to realize the following milestones during 2020:

- Expand test volume through its work with independent practices, employers, and first responders
- Expand its telehealth initiative through increasing digital advertising, adding more tests to the telehealth offering, and improving the online user experience through new technologies
- Continue to support Oncore Pharma and Coastal Medical in their efforts for domestic and global distribution of the Company's products
- Announce the inclusion of StageZero tests on the Mercer VIP platform
- Complete test implementation planning and commence test offering with a large healthcare system
- Initiate extensive screening programs with large employers of high-risk personnel
- Retain an independent research firm to help formulate future financial strategies
- Launch investor relations campaign to attract new investors, including the addition of monthly newsletter
- Continue clinical validation of Aristotle™

Intellectual Property

To protect its intellectual property rights, StageZero relies on a combination of patent applications, copyrights, trademarks, trade secret laws, as well as confidentiality, material data transfer agreements, licenses, and invention assignment agreements. The Company further relies upon unpatented trade secrets and improvements, unpatented know-how, and continuing technological innovation to develop and maintain a competitive position. Figure 2 summarizes the Company's current intellectual property positions.

Figure 2
INTELLECTUAL PROPERTY

GeneNews Ref No.	Serial Number	Publication Number	Patent Number	Sunstein's Ref No./Foreign Agent Reference No.	Filing Date	Issued Date	Estimated Expiration Date	Application Status is Expired	Title	Inventors
FOUNDATIONAL PATENT FAMILY - Identifying Biomarkers of Disease by Measuring RNA in Blood										
US										
CG10-CH001	12/757,918	US 2011/0003294 A1	8,067,173	3907.1025	9-Apr-10	29-Nov-11	4-Jan-20	26-Mar-20	METHOD OF PROFILING GENE EXPRESSION IN A HEALTHY SUBJECT	C.C. Liew
CG10-CD001	12/757,914	US 2011/0008779 A1	8,101,358	3907.1024	9-Apr-10	24-Jan-12	4-Jan-20	26-Mar-20	METHOD OF PROFILING GENE EXPRESSION IN A SUBJECT HAVING DISEASE	C.C. Liew
CG10-CT001	12/757,921	US 2011/0003295 A1	8,114,597	3907.1026	9-Apr-10	29-Nov-11	4-Jan-20	26-Mar-20	METHOD OF PROFILING GENE EXPRESSION IN A SUBJECT UNDERGOING TREATMENT	C.C. Liew
CG10-D03	12/757,928	US 2011/0003296 A1	8,133,674	3907.1029	9-Apr-10	13-Mar-12	4-Jan-20	26-Mar-20	METHOD OF PROFILING GENE EXPRESSION IN A SUBJECT HAVING DIABETES	C.C. Liew
CG10-D04	12/757,930	US 2011/0003297 A1	8,148,072	3907.103	9-Apr-10	3-Apr-12	4-Jan-20	26-Mar-20	METHOD OF PROFILING GENE EXPRESSION IN A SUBJECT HAVING HEART FAILURE	C.C. Liew
CG10-D05	12/757,931	US 2011/0003298 A1	8,110,358	3907.1031	9-Apr-10	7-Feb-12	4-Jan-20	26-Mar-20	METHOD OF PROFILING GENE EXPRESSION IN A SUBJECT HAVING PROSTATE CANCER	C.C. Liew
CG10-D06	12/757,934	US 2011/0014614 A1	8,133,675	3907.1032	9-Apr-12	13-Mar-12	4-Jan-20	26-Mar-20	METHOD OF PROFILING GENE EXPRESSION IN A SUBJECT HAVING INFECTIOUS DISEASE	C.C. Liew
Colon Cancer (Colon Sentry)										
US										
CG121US	12/384,914		8,921,074	3907.101	10-Apr-09	30-Dec-14	16-Jan-30		METHOD AND APPARATUS FOR DETERMINING A PROBABILITY OF COLORECTAL CANCER IN A SUBJECT	Samuel CHAO C.C. LIEW

Source: US Patent and Trademark Office.

Rather than owning all of the intellectual property on which it relies, StageZero licenses certain intellectual property and is substantially dependent on such licenses in order to market and sell its products. In the event that the licensor of any license the Company holds files a petition in bankruptcy, there can be no assurance that the rights under the Company's licenses will not be curtailed or otherwise affected, even if the Company actively pursues enforcement of the license agreement. If a licensor files for bankruptcy, among other consequences, the licensed intellectual property may be sold to a third party and such sale may extinguish StageZero's rights under any existing license agreements. This could cause a significant hardship for the Company as the licensee and, as a result, have a material adverse effect on StageZero's business.

StageZero's current patent portfolio is focused around its core technology, the Sentinel Principle®, and its lead product, ColonSentry®. The patents are protected in key current and potential future marketing jurisdictions, including the U.S. and Canada. The Company also has six core trademarks (both registered and pending), including the Company's house mark and families of marks built around the Sentinel Principle® and ColonSentry®, many of which are being protected in multiple jurisdictions.

All employees and technical consultants working for the Company are required to execute confidentiality agreements in connection with their employment and consulting relationships. Confidentiality agreements provide that all confidential information developed or made known to others during the course of the employment, consulting, or business relationships shall be kept confidential, except in specified circumstances. Agreements with employees provide that all inventions conceived by the individual while employed by the Company are the Company's exclusive property.

Core Story

StageZero Life Sciences, Ltd ("StageZero" or "the Company") is an innovator in the liquid biopsy space focused on the early detection of cancer and multiple disease states through blood tests. The Company develops and commercializes innovative diagnostic solutions that reduce the incidence of late stage cancer and can aid in the detection of cancer at the earliest possible stage (Stage 0).

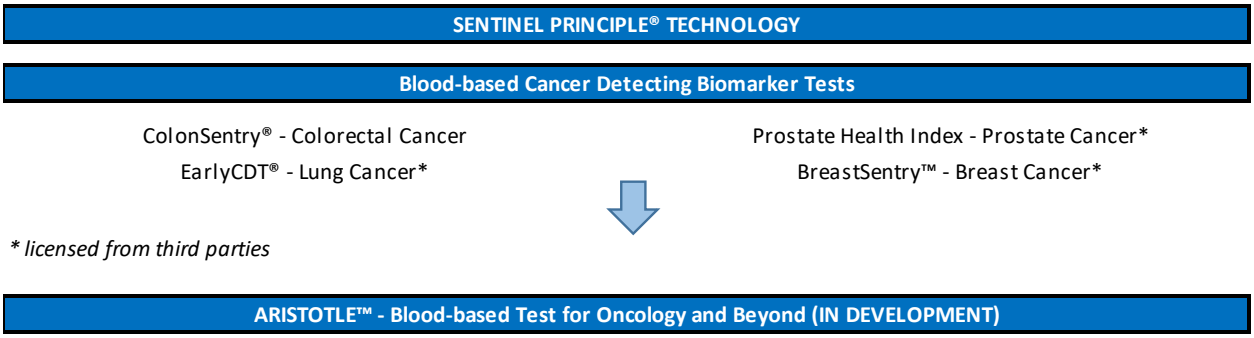
The Company's proprietary Sentinel Principle® technology platform is a gene expression technology that uses a blood sample to detect cancer in the early stages. The technology is based on the scientific observation that circulating blood reflects, in a detectable way, what is occurring throughout the body. The science behind the Sentinel Principle® led to the development of the Company's flagship product, ColonSentry®, a blood-based test for assessing an individual's current risk of having colorectal cancer (CRC). In addition, StageZero offers early cancer diagnostics and risk stratification tests used to identify the probability of having four of the most prevalent cancers: colorectal, lung (*Early*CDT®-Lung), prostate (Prostate Health Index [*phi*]), and breast cancer (BreastSentry™), through several novel, proprietary molecular diagnostic platforms.

StageZero's first commercialized test to use the Sentinel Principle®—ColonSentry®—was also one of the first blood-based biomarker tests for the early identification of CRC. ColonSentry® validation in over 10,000 patient samples also serves as a test of concept for the Company's Sentinel Principle® technology. Since launch in 2014, ColonSentry® has been used successfully in over 100,000 patients in the U.S.

Utilizing its Sentinel Principle® technology, StageZero is developing Aristotle™, its next generation test. Aristotle™ is a multi-cancer panel for the simultaneous screening of 10 cancers (colorectal, prostate, cervical, endometrial, breast, ovarian, liver, bladder, nasopharyngeal, and stomach cancer) from a single sample of blood, with high **sensitivity** and **specificity** for each cancer. Furthermore, the Company is planning to expand the applications of Aristotle™ beyond oncology to aid in the diagnosis of disease states in gastroenterology, neurology, cardiology, and autoimmune disorders. Figure 3 provides a snapshot of the Company's product portfolio.

Figure 3

STAGEZERO'S PRODUCT PORTFOLIO



Sources: StageZero Life Sciences, Ltd. and Crystal Research Associates.

In addition to building a pipeline of products for early cancer detection, the Company operates a CAP-accredited and CLIA-certified reference laboratory based in Richmond, Virginia that offers the ColonSentry® test as well as licensed biomarker tests for lung, breast, and prostate cancers.

CANCER DIAGNOSTICS

Cancer is a major burden of disease and among the leading causes of death worldwide. In 2019, there were an estimated 18.1 million new cases and 9.6 million cancer-related deaths globally. As population aging continues, cancer is expected to remain a significant health problem as the leading cause of death and the most important barrier to increasing life expectancy (Source: *CA: A Cancer Journal for Clinicians*; Vol. 68 (6): 394-424, 2018).

In 2020, more than 1.8 million new cancer cases are expected to be diagnosed in the U.S.—equivalent to more than 4,900 new cases each day—with 606,520 deaths (translating into about 1,660 deaths per day). Cancer is the second most common cause of death in the U.S., exceeded only by cardiovascular disease. However, due to the significant improvements in treating and preventing cardiovascular disease, cancer is expected to become the number one cause of death in the U.S. (Source: American Cancer Society's *Cancer Facts & Figures 2020*). As seen in Figure 4, cancers of the lung, colorectum, breast, and prostate are the most common types with the highest mortalities.

Figure 4

CANCER STATISTICS

Estimated New Cases

Males			Females		
Prostate	191,930	21%	Breast	276,480	30%
Lung & bronchus	116,300	13%	Lung & bronchus	112,520	12%
Colon & rectum	78,300	9%	Colon & rectum	69,650	8%
Urinary bladder	62,100	7%	Uterine corpus	65,620	7%
Melanoma of the skin	60,190	7%	Thyroid	40,170	4%
Kidney & renal pelvis	45,520	5%	Melanoma of the skin	40,160	4%
Non-Hodgkin lymphoma	42,380	5%	Non-Hodgkin lymphoma	34,860	4%
Oral cavity & pharynx	38,380	4%	Kidney & renal pelvis	28,230	3%
Leukemia	35,470	4%	Pancreas	27,200	3%
Pancreas	30,400	3%	Leukemia	25,060	3%
All Sites	**893,660**	**100%**	**All Sites**	**912,930**	**100%**

Estimated Deaths

Males			Females		
Lung & bronchus	72,500	23%	Lung & bronchus	63,220	22%
Prostate	33,330	10%	Breast	42,170	15%
Colon & rectum	28,630	9%	Colon & rectum	24,570	9%
Pancreas	24,640	8%	Pancreas	22,410	8%
Liver & intrahepatic bile duct	20,020	6%	Ovary	13,940	5%
Leukemia	13,420	4%	Uterine corpus	12,590	4%
Esophagus	13,100	4%	Liver & intrahepatic bile duct	10,140	4%
Urinary bladder	13,050	4%	Leukemia	9,680	3%
Non-Hodgkin lymphoma	11,460	4%	Non-Hodgkin lymphoma	8,480	3%
Brain & other nervous system	10,190	3%	Brain & other nervous system	7,830	3%
All Sites	**321,160**	**100%**	**All Sites**	**285,360**	**100%**

Source: CA: a Cancer Journal for Clinicians, Cancer Statistics 2020.

Cancer also represents a significant economic burden. The cost of cancer care is expected to reach almost $174 billion by 2020, with costs likely to rise as the population ages and cancer prevalence increases. Costs are also expected to increase as new, and often more costly, treatments are adopted as standards of care (Source: U.S. National Institutes of Health's National Cancer Institute). Cancer further represents the leading catastrophic claim for employers, representing over one quarter (26.7%) of all stop-loss claim reimbursements, with a small number of late stage cancer claims causing the majority of costs. In 2016, claims exceeding $1 million dollars were only 2.2% of total claimants but accounted for 23% of total stop-loss claims reimbursement (Source: *2017 Sun Life Stop-Loss Research Report*).

Importance of Early Diagnosis

Cancers can be diagnosed at different stages in their development. Stage of cancer diagnosis may be expressed as numbers (for example I, II, III, or IV) or by terms such as localized (cancer is limited to the place where it started), regional (cancer has spread to nearby lymph nodes, tissues, or organs), and distant (cancer has spread to distant parts of the body). The lower the number or the more localized the cancer, the better a person's chances of benefiting from treatment. Early detection has been proven to improve survival rates and quality of life, decrease the cost of treatment, and reduce the complexity of the therapeutic regimen. When a cancer is detected at an early stage, the chance of survival beyond five years is higher than when detected at a later stage. For example, more than 90% of women diagnosed with the earliest stage of ovarian cancer survive their disease for at least 5 years, compared to around 29% for women diagnosed at the most advanced stage of the disease.

Detecting cancer early also greatly reduces cancer's financial impact; not only is the cost of treatment lower in cancer's early stages, but people can also continue to work and support their families while undergoing treatment. Studies in high-income countries show that treatment costs for early-diagnosed patients are two to four times less expensive than treatment for those diagnosed with advanced-stage cancer (Source: The Asco Post's *World Cancer Day 2019: Emphasis on Early Detection*, February 2019).

A U.S. study estimates the national cost savings from early diagnosis at $26 billion per year. When focusing on breast, lung, prostate, colorectal cancers, and melanoma—the top five cancers by incidence, representing 50.87% of all cancers—the estimated costs of treatment adds up to over $67 billion and the corresponding estimated cost-savings from early diagnosis adds up to over $10.7 billion or 41.49% of total cost-savings for all cancers (Source: *Data*, Vol. 2 (3): Estimating Cost Savings from Early Cancer Diagnosis, 2017). Despite these numbers, a high number of cancers are detected in advance stages after symptoms appear, with 40% of screenable cancers diagnosed in late stages. Figure 5 shows the percentage of selected cancers detected in late stages (i.e. regional and distant stages).

Figure 5

PERCENTAGE OF SELECTED CANCERS DETECTED IN THE REGIONAL AND DISTANT STAGES

Colorectal Cancer	56%	Ovarian Cancer	79%
Breast Cancer	37%	Cervical Cancer	51%
Lung Cancer	79%	Prostate Cancer	17%

Source: CA: a Cancer Journal for Clinicians, Cancer Statistics 2020.

Effect of Early Diagnosis on Survival Rate and Treatment Cost

Early detection has a direct correlation with survival rates and cost of care in all cancers. Diagnosis of cancer in early stages is associated with better clinical and survival outcomes, as well as lower costs of treatment. Figure 6 provides the 5-year survival rate for the most common cancer types according to its stage at detection, as well as the annualized cost of care during the first-year post disease diagnosis.

Figure 6

SURVIVAL RATE AND TREATMENT COSTS

5 YEAR Survival Rate			
	Localized	**Regional**	**Distant**
Colorectal	90%	71%	14%
Lung	57%	31%	5%
Prostate	>99%	>99%	31%
Breast	99%	86%	27%

Annual Cancer Treatment Costs		
	Early Stage	**Late Stage**
Colorectal	$33,000	$120,000
Lung	$34,000 (2 year)	$240,000 (1 year)
Prostate	$4,300	$100,000
Breast	$82,000	$134,000

Sources: American Cancer Society, American Health and Drug Benefits.

Breast and Prostate Cancer

Early detection is key in breast and prostate cancer prognosis. Five-year survival for breast and prostate cancer patients with early stage disease is 99% and ~100%, respectively, and survival rates remain high at 10 years. However, that figure decreases to 27% and 31% for 5-year survival if the cancer is detected at a late stage (Source: American Cancer Society's *Cancer Facts & Figures 2020*).

Stage at diagnosis also affects treatment cost. Analysis of 11 studies determined that the treatment costs for breast cancer at Stage II, III and IV were 32%, 95%, and 109% higher than Stage I, respectively. Furthermore, analysis of five studies found that the mean treatment costs of regional and distant breast cancer were 41% and 165% higher than for local breast cancer (Source: *PLoS One*, Vol. 13(11), 2018). Another study found that the average costs per patient allowed by the insurance company in the year after diagnosis were $60,637, $82,121, $129,387, and $134,682 for disease stage 0, I/II, III, and IV, respectively (Source: *American Health Drug Benefits*, 9(1): 23–32,2016). A similar increase is seen in prostate cancer, where treatment costs goes from $4,300 for the first year for a cancer that is diagnosed in earlier stages, to over $100,000 for a late stage cancer.

Lung Cancer

Lung cancer is a major global killer due to its high mortality rate and late diagnosis. Over half of new patients are diagnosed after the cancer has spread, which results in a 5-year survival rate of only 4% (Source: *Canary Foundation's Early Detection Facts and Figures*). Treatment costs also go up significantly, from $34,000 for the first two years of treatment for a cancer that is diagnosed in earlier stages, to over $240,000 for the first year of treatment for a late stage cancer.

Colorectal Cancer (CRC)

Similar numbers are found when dealing with CRC. CRC detected early has 90% 5-year survival rate, compared to only 14%-15% survival rate if it is caught late and has spread to other organs (Source: American Cancer Society's *Cancer Facts & Figures 2020*). Cost of treatment also surges with late diagnosis, rising from $33,000 to $120,000 for the first year of treatment.

SHORTCOMINGS OF CURRENT SCREENING OPTIONS

Regular cancer screening, following recommendations for the type, age, lifestyle, and personal risk, contributes to earlier detection and increases the likelihood of successful treatment. For women at average risk for cervical and breast cancers, an annual **PAP (Papanicolaou) test** beginning at age 21 and an annual mammography beginning at age 40 are recommended. Preventive CRC screening for men and women at average risk include an annual **fecal occult blood testing (FOBT)**, **sigmoidoscopy** every 5 years, and colonoscopy every 10 years beginning at age 50. In addition, the U.S. Preventive Services Task Force (USPSTF) recommended annual screening for lung cancer with low-dose computed tomography (LDCT) for people aged 55 to 80 years who have a current or past smoking history within the last 15 years.

Despite the availability of cancer screening tests, patients are not adhering to preventive screening guidelines, as shown in Figure 7. Among women aged 50 to 74, only 71.7% reported a recent mammogram. In CRC, more than a third of the high-risk population is non-compliant, with only 63.4% of women and 61.9% of men aged 50 to 75 reporting a recent CRC screening. The numbers are worse for prostate and lung cancer. Among men aged 50 years or older, only 35.8% reported having a PSA test in the past year (Source: *Preventing Chronic Diseases'* Volume 15 (E97), 2018). In lung cancer, a recent study found that only 3.9% of high-risk smokers in the U.S. received their recommended low-dose computed tomography (LDCT) screening (Source: *JAMA Oncology*, Vol. 3(9):1278-1281, 2017).

Figure 7
SCREENING COMPLIANCE

Breast	71.7%
Colorectal Men	61.9%
Colorectal Women	63.4%
Prostate	35.8%
Lung	3.9%

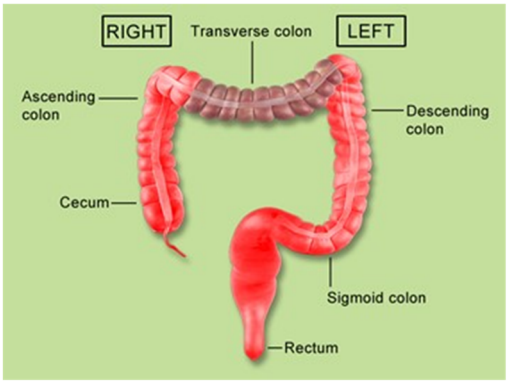
Sources: JAMA Oncology and Preventing Chronic Diseases.

The non-compliance of screening guidelines has a significant impact on mortality rates. An estimated 70% of CRC deaths come from patients that were not up to date in screening for the condition, according to a Kaiser Permanente study (Source: Gastroenterology and Endoscopy News' *Analysis of Failures Shows Limits of CRC Screening Efforts*, 2018). In addition, a recent study found that LDCT screening decreased lung cancer mortality by as much as 61% in at-risk women and 26% for high-risk men, yet less than 4% of heavy smokers actually undergo the scanning procedure (Source: Advisory Board's *Lung cancer screening works. But how can we increase compliance?* 2018). The problem is further compounded by the fact that the current cancer screening methods are not perfect.

Gaps in Current Screening—Colorectal Cancer

There are a variety of CRC screening and diagnostic methods in use today, including colonoscopy, FOBT, and virtual colonoscopy. In the U.S., colonoscopy is the most commonly used method for CRC screening. Unlike other screening tests used to detect early-stage CRC, colonoscopy can often prevent it by removing polyps from the colon before they become cancerous. Widespread uptake of colonoscopy (and other colon cancer screening tests) has led to a steep decline in colon cancer incidence rates.

Figure 8
COLON



Source: Medscape.

While still an effective screening and detection tool, colonoscopy has several important limitations. Some of these limitations can be patient-specific—inadequate patient pre-procedure preparation, which can occur in up to 25% of cases, can limit the effectiveness of the screening tool. Other limitations can be physician-based, as experience can lead to higher polyp detection rate (Source: *Journal of Cancer,* Vol. 4 (3):217-226, 2013).

But most experts agree than the greatest shortfall of colonoscopies is that although the procedure does a good job of detecting early signs of disease on the left side of the colon (shown in Figure 8), it is not as effective at spotting potential problems on the right side of the organ. A study found that colonoscopy was strongly linked to a significant lower death rate related to CRC on the left side of the organ, but it showed virtually no death-prevention benefit with right-sided CRC (Source: *Gastroenterology and Hepatology*, Vol. 6(7): 428–430, 2010).

Anatomical location of the tumor also affects its behavior, as tumors in the proximal colon (right side) and distal colon (left side) exhibit different histology and molecular characteristics. Left-sided tumors have polypoid morphology, making them easier to detect. In contrast, right-sided CRC have flat morphology that is difficult to detect (Source: *Gastroenterology Research*, Vol. 11(4): 264–273, 2018). The inability of colonoscopies to fully detect right side lesions gets compounded by the fact that several studies in recent years have shown that patients with CRC on the right side have worse short and long-term survival rates than those with left-sided tumors, regardless of the stage of the disease at diagnosis.

Overall five-year survival for patients with right-sided tumors was 66% for stage II disease and 56% for stage III. In comparison, survival rates were 70% and 60% for patients with left-sided stage II and III cancers (Source: Science Daily's *Right-Sided Colon Cancer Patients Have Poorer Survival Than Those With Left-Sided Disease*, 2018). Other screening options, such as sigmoidoscopy and stool test, are less capable (or even unable) of detecting right sided lesions when compared to colonoscopies.

These shortcomings can result in **interval cancers**, which occur in a given time period (typically three or five years) after a colonoscopy is performed but before the next colonoscopy is scheduled. The 2012 guidelines of the U.S. Multi-Society Task Force on Colorectal Cancer, which includes the American College of Gastroenterology, the American Gastroenterological Association, and the American Society for Gastrointestinal Endoscopy, reports that up to 9% of cancers in the cancer registries were interval cancers, with patients having had a colonoscopy in the six to 36 months prior to their CRC diagnosis. These cancers are more likely to occur on the right side than the left side of the colon, and researchers believe that the most common reason for interval cancers are lesions that may have been overlooked at the time of colonoscopy (Sources: University of Utah, and *Gastroenterology and Hepatology*, Vol. 6(7): 428–430, 2010).

Gaps in Current Screening—Lung Cancer

The use of LDCT as a screening tool for lung cancer is recommended by the USPSTF. Early diagnosis by LDCT screening has been linked to a substantial reduction in the rate of lung cancer mortality. However, its limitations center on the possibility of **overdiagnosis**, its false-positive rate, and the possibility of complications from invasive follow-up. In a recent study, 18.5% of lung cancers identified would not impact the patient's lifespan if left untreated and might reflect overdiagnosis. In addition, LDCT identifies both malignant and benign non-calcified nodules, the latter often being called false positives. Most studies reported that >90% of nodules detected were benign (Source: *Oncology Research and Treatment*, Vol. 37 (3):58-66, 2014).

Despite these shortcomings, due to the high mortality of lung cancer and the proven effect of lowering mortality of the LDCT test, the biggest limitation of lung cancer screening is the low participation of at-risk patients, with less than 4% of heavy smokers actually undergoing the scanning procedure. Barriers that limit participation in screening programs are complex and multifactorial. The main barrier seems to be emotional, as current smokers are less likely to undergo the screening procedure than past smokers. However, other factors, such as difficulties with traveling to attend screening, career responsibilities, and costs were the most common self-reported reasons for non-participation in screening programs. Thus, the development of a screening test that lowers the barriers of participation is a key element on improving the outcome of patients with the disease (Source: *Public Health Reviews,* Vol. 39 (23), 2018).

Gaps in Current Screening—Prostate Cancer

A common screening technique used for prostate cancer is prostate-specific antigen (PSA) blood test. The PSA test measures the level of the PSA protein which is made by cells in the prostate. Using PSA as a screening technique has significant shortcomings: (1) PSA is produced by prostate cells whether the cells are cancerous or not; thus people with larger healthy prostates produce more PSA; (2) PSA levels cannot differentiate between prostate cancer and benign less dangerous conditions, such as **benign prostatic hyperplasia (BPH)**; (3) PSA cannot reliably tell the difference between slow-growing cancers that do not pose a risk and less common, potentially deadly cancers. Men with harmless cancers may then be subjected to unnecessary biopsy and treatments that may cause side effects such as impotence, incontinence, or bowel dysfunction; and (4) a normal PSA level (i.e., 4 ng/ml or below) does not guarantee a cancer-free prostate; in approximately 15% of men with a normal PSA levels, a biopsy reveals prostate cancer (Source: Harvard Health Publishing's *The pros and cons of PSA Screening*).

Screening for cancer is generally thought to be a good thing, but once the risks outweigh the benefits, the test may actually be doing more harm than good. Due to these concerns about overdiagnosis and overtreatment, in 2012, the USPSTF discouraged PSA screening in healthy low-risk men. Although experts are somewhat split on the value of PSA tests as a screening tool, there is widespread belief that there is an urgent need to refine PSA testing to be a more effective screening tool (Source: University of Chicago Medicine's *Screening for prostate cancer: Are PSA blood tests reliable?* July 2018).

Gaps in Current Screening—Breast Cancer

A similar situation occurs for breast cancer. Mammograms are the best breast cancer screening tests available, but they also have their limitations. Overall, screening mammograms miss 20% of breast cancers (1 in 5), especially in women with dense breasts. In addition, the risk of a false positive mammogram, where the mammogram looks abnormal even though no cancer is actually present, is significant, with approximately half of the women getting annual mammograms over a 10-year period expected to have a false-positive finding. Abnormal mammograms require extra testing (diagnostic mammograms, ultrasound, and sometimes MRI or even a breast biopsy) to find out if the change is cancer (Source: American Cancer Society's *Limitations of Mammograms*).

LIQUID BIOPSIES FOR CANCER

Liquid biopsy is a minimally invasive technology based on the sampling and analysis of non-solid biological tissue, primarily blood, which detects rare disease-specific biomarkers. Liquid biopsy oncology applications use an array of sensitive assays capable of detecting cancer cells, tumor DNA, gene expressions, proteins, and other specific tumor-derived substances and materials that are circulating in the blood.

Liquid biopsies have significant advantages over traditional invasive biopsies, primarily based on its non-invasive and simple procedure, as shown in Figure 9. Liquid biopsies bypass the need for invasive and costly needle or surgical tissue biopsy, which could lead to pain and complications. Traditional tissue biopsies range in cost from $15,000 to $60,000 U.S. dollars, depending on whether invasive surgery is required, the level of sample preparation, pathology services, and follow-on genetic tests. Because so many hands are in play, traditional biopsies have a failure rate of approximately 25% (Source: Technology Networks' *Liquid Biopsies: Miracle Diagnostic or Next New Fad?* 2016). Furthermore, different screening and diagnostic tests present large variability in compliance. Blood test have a high compliance rate, especially helpful for patients who refuse screening or patients in the diagnostic gap.

Figure 9

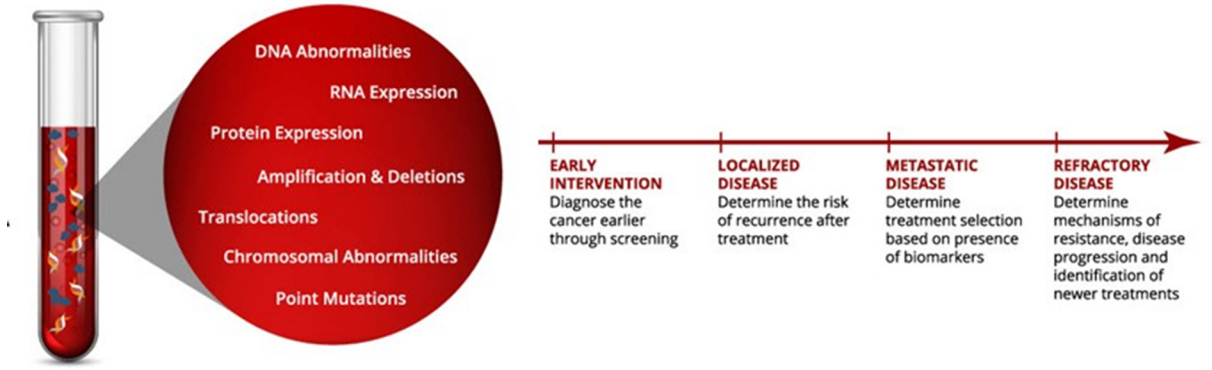
LIQUID BIOPSY COMPARISON

LIQUID BIOPSY	STANDARD BIOPSY
Minimally invasive	Invasive
Minimal pain/risk	Some pain/risk
Easily obtained	Not easily obtained
Comprehensive tissue profile	Localized sampling of tissue
Time intensive and costly	Quick and low cost
Screening applications	Limited or non-existent screening applications

Source: My Cancer Genome.

The benefits of liquid biopsies extend to its applications, as shown in Figure 10 (page 19). A liquid biopsy may be used to help find cancer at an early stage (screening), to help plan treatment, or to validate the efficiency of a cancer treatment (as the ability to take multiple samples of blood over time may help doctors understand what kind of molecular changes are taking place within a tumor or assess a patient's response over the course of treatment), and can help physicians monitor for disease recurrence or relapse (Source: College of American Pathologists' *The Liquid Test*).

Figure 10
LIQUID BIOPSY APPLICATIONS



Source: Healio.

Liquid Biopsy Cancer Screening Overview

The ability of a cancer to progress to late stages without the appearance of symptoms is one of the main reasons for the prevalence of late stage cancer diagnostics. The development of an effective and simple screening test that identifies cancer in asymptomatic individuals can have a significant impact in reducing the morbidity or mortality of the different types of cancer (Source: *Translational Cancer Research,* Vol 7, Supplement 2, 2018).

Liquid biopsy oncology technologies are mainly used as a diagnostic and monitoring tools. Liquid biopsies have also been suggested as a possible screening method for early cancer detection. Because of the limited amount of tumor-related materials present in the blood in the earlier stages of the disease, liquid biopsy screening is considered the most difficult application, but it also has the greatest potential to reduce morbidity and mortality from cancer (Source: *Science Translational Medicine*, Vol. 11, Issue 507, 2019). Thus, liquid biopsy screening validity is directly correlated to its ability to display a high sensitivity, which is the ability of the test to identify correctly those who have that disease, and a high specificity, reflecting its capacity to identify correctly those who do not have the disease (Source: *Translational Cancer Research,* Vol 7, Supplement 2, 2018).

Sensitivity, also called true positive rate, measures the proportion of actual positives that are correctly identified as such, or how often a test correctly generates a positive result for people who have the condition that is being tested for. Low sensitivity leads to **false negatives**, where the patient with the condition is given a clean bill of health.

Specificity, also called a true negative rate, measures the proportion of actual negatives that are correctly identified as such (e.g., the percentage of healthy people who are correctly identified as not having the condition). Low specificity leads to false positive, where a person is incorrectly told they have the particular disease, creating anxiety and needless, sometimes invasive, procedures. Much of the controversy surrounding current screening tests, such as mammography and PSA, is based on the high ratio of false positives to true positives, due to the low specificity of those procedures (Source: *Science Translational Medicine*, Vol. 11, Issue 507, 2019).

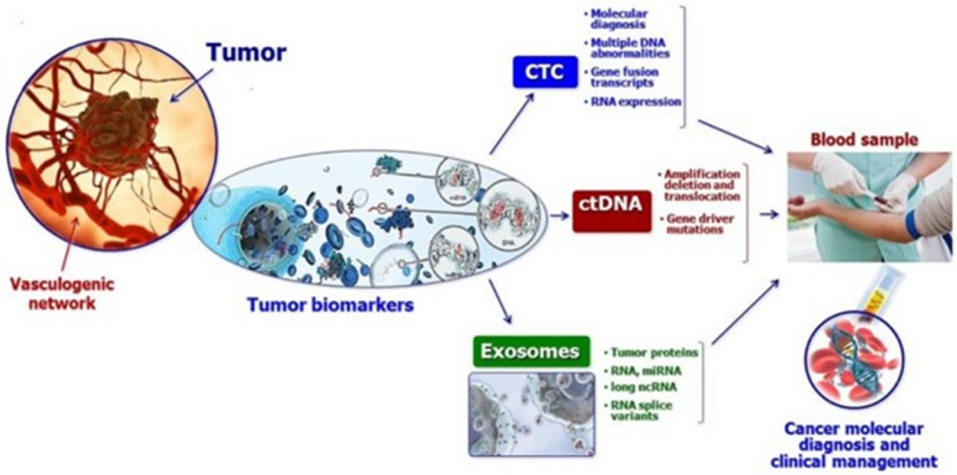
Liquid Biopsy Cancer Screening Technologies

A way to improve the sensitivity and specificity of liquid biopsy technologies is to develop reliable biomarkers to detect circulating cells or traces of the cancer's **ribonucleic acid (RNA)** or DNA in the blood. The new biomarkers rely on the fact that apoptotic or necrotic cancer cells release tumor cells (CTC), circulating tumor DNA fragments (ctDNA), as well as **exosomes**—membrane-encapsulated subcellular structures containing proteins and nucleic acids—into the blood stream. Detection, identification, and assessment of these tumor-derived components from peripheral blood represent the basis for liquid biopsy oncology applications. Specifically, the liquid biopsy's biomarkers most commonly used include the following, as seen in Figure 11 (page 20):

- circulating tumor cells (CTCs);
- circulating free tumor DNA (ctDNA); and
- extracellular micro-vesicles (including exosomes) containing small-RNA and DNA.

Figure 11

LIQUID BIOPSY TECHNOLOGIES



Source: Therapeutic Advances in Medical Oncology.

The initial limitations related to the scarcity of the tumor derived material as well as the difficulty in distinguishing between normal and tumor representing levels has been overcome by the increased sensitivity of next-generation sequencing (NGS) techniques, opening the door for the expansion of liquid biopsy applications (Source: *Therapeutic Advancements in Medical Oncology*, Vol.10; 2018).

CTC

Circulating tumor cells (CTCs) are those cells present in blood circulation that possess antigenic and/or genetic characteristics of a specific tumor type. CTCs are shed from either primary or secondary tumor sites into the circulatory system and are responsible for the development of distant metastases. Cumulative evidence indicates that primary cancers begin shedding neoplastic cells into the circulation at an early stage. Because CTCs' biological characteristics are often different from those of their respective primary cell populations, they provide an ideal approach to molecular cancer diagnosis and treatment options, and their investigation is widespread in cancer research. However, their low frequency and difficulty of being isolated provides limitations to their use as a screening tool (Source: *Therapeutic Advancements in Medical Oncology*, Vol.10; 2018).

Despite these issues, studies of the use of CTCs in screening and early diagnostic applications have provided some encouraging results. For example, a study showed that a CTC count above a specific threshold had a high sensitivity (89%) and specificity (100%) for the differentiation between benign and malignant disease (Source: *Translational Cancer Research*, Vol 7, Supplement 2, 2018). In the past decade, technology to detect, capture, and profile CTCs and nucleic acid has advanced rapidly, leading to an improve capacity for the detection of CTCs in peripheral blood. This has facilitated their use on cancer screening applications.

ctDNA

Circulating tumor DNAs (ctDNA) are tiny fragments of DNA in the blood that break away from tumors. When tumor cells die, they release ctDNA into the blood. Cancer mutations in ctDNA mirror those found in traditional tumor biopsies, which allow them to be used as molecular biomarkers to track the disease. Scientists can then analyze ctDNA using next-generation sequencing (NGS) or polymerase chain reaction (PCR)-based methods. Next-generation sequencing (NGS)-based methods provide a comprehensive view of a cancer's genetic makeup and are especially useful in diagnosis, while digital PCR offers a more targeted approach and are especially well-suited for detecting minimal residual disease and for monitoring treatment response and disease progression.

The expected cancer-specificity of mutations also makes ctDNA an attractive biomarker for early detection of cancer, but massively parallel sequencing is too error prone to dependably identify rare mutant ctDNA among abundant regular DNA. ctDNA is only one type of DNA circulating in the blood. Pregnant women have DNA from their baby's placenta in their blood. People who've had a heart attack or stroke may also have DNA fragments in their blood. Collectively, all those DNA fragments are called cell-free DNA. Therefore, researchers must be able to accurately identify ctDNA among all the other types of DNA in the blood. The amount of ctDNA in the blood in early-stage cancer is very low and can constitute only 0.01% of the total cell free DNA, as early-stage tumors (and even some medium-sized tumors) are known to release very little DNA. Because of this, a ctDNA-based test, though specific, would not be sufficiently sensitive.

On the other hand, protein quantification, known to be elevated when cancer is present, is highly sensitive although not highly specific. In order to improve the combined sensitivity and specificity of liquid biopsies for early cancer diagnosis, researchers have been combining ctDNA with protein detection. The resulting ctDNA and protein combination liquid biopsy proved to have greater specificity and sensitivity for earlier cancer detection (Source: Technology Networks' *Recent Advances in Liquid Biopsy for Cancer*, 2019).

<u>CancerSEEK</u>

The dual ctDNA and protein principle was applied by researchers at Johns Hopkins for the creation of CancerSeek, a liquid biopsy screening application for several types of cancer, including ovarian, liver, stomach, pancreatic, esophageal, colorectal, lung, and breast. CancerSEEK detects mutations in the top 16 most mutated genes across the cancer panel, combined with quantification of eight known protein markers for several common types of cancer. While the DNA tests would detect the presence of cancer, the protein analysis could pinpoint where the cancer was located. Their ability to pin down the cancer's location varied based on where it started in the body. On a study with 1,005 patients who had been diagnosed with stage I to III cancers of the ovary, liver, stomach, pancreas, esophagus, colorectum, lung, or breast, CancerSEEK demonstrated a median sensitivity of 70% (lowest for breast cancer at 33%, highest for ovarian cancer at 98%) with a specificity higher than 99% for all tested cancers, as only 7 of 812 healthy controls scored positive (Source: *Science*, Vol. 359(6378):926-930, 2018). John Hopkins has licensed the CancerSeek technology, along with a foundational DNA sequencing technology, Safe-SeqS, and a suite of supporting biomarker technologies, to Thrive Earlier Detection Corp., a new company that launched with a $110 million in Series A funding. Thrive's main business is the continued development and commercialization of CancerSeek.

miRNA

MicroRNAs (miRNAs) are a class of small noncoding RNA molecules which are involved in the regulation of gene expression by degrading or silencing their target mRNAs and/or inhibiting their translation. Most of the mRNA present in blood is packaged in microvesels (e.g., exosomes), which provide them with protection from degradation. Numerous diseases and disorders, such as tumors, cardiovascular diseases, multiple sclerosis, and liver injury have been associated with altered extracellular miRNA profiles (Source: *Nucleic Acids Research*, Vol.44(13):5995-6018, 2016). Furthermore, the therapeutic relevance of miRNAs was studied in the blood of patients with different types of cancer. Quantities and species of miRNAs were shown to fluctuate in the presence of malignant and non-malignant disease. Of note, several miRNA signatures have been proposed for the diagnosis of different cancer types (lung, ovary, breast, prostate, liver, colorectal, brain, melanoma, pancreas, etc.) (Source: *EbioMedicine,* Vol. 5:4–6, 2016).

StageZero Products

StageZero Life Sciences is focused on developing and commercializing proprietary molecular diagnostic tests for early detection of diseases and for personalized health management, with a primary focus on cancer-related indications. The Company has developed an innovative approach to identifying unique **messenger RNA (mRNA)**-based biomarkers from whole blood. It's proprietary technology platform—called the Sentinel Principle®—has the ability to detect a large number of diseases and medical conditions from a single blood sample. Stage Zero, through its Sentinel Principle®, is one of the founders of the liquid biopsy principle.

The science behind the Sentinel Principle® led to the development of the Company's flagship product, ColonSentry®, a blood-based test for assessing an individual's current risk of having colorectal cancer. Furthermore, StageZero offers early cancer diagnostics and risk stratification for colorectal, lung, prostate and breast cancer, through several novel, proprietary molecular diagnostic platforms. In addition to building a pipeline of products for early cancer detection, the Company operates a CAP-accredited and CLIA-certified reference laboratory in Richmond, Virginia, that performs the sample processing for the ColonSentry® test as well as the licensed biomarker tests for lung, breast, and prostate cancers.

THE SENTINEL PRINCIPLE® TECHNOLOGY PLATFORM

StageZero's proprietary Sentinel Principle® technology platform is a gene expression (mRNA) technology that uses a blood sample to detect cancer in early stages. The Sentinel Principle® is based on the scientific observation that circulating blood cells reflect, in a detectable way, what is occurring throughout the body.

As blood circulates, communication occurs between cells in blood and tissue. As a result of the continuous interactions between blood and body cells, different clinical conditions, including subtle changes occurring in association with injury or disease, generate specific and detectable changes in gene expression of blood cells reflective of the initiating stimulus. These changes can then be capitalized on as biomarkers for screening and diagnostic purposes.

Clinical studies have demonstrated that monitoring gene expression in blood can be used to develop gene expression signatures reflective of over 35 different conditions and diseases in human subjects. Alterations in expression profiles were characteristic of a wide array of diseases, including many forms of cancer, heart failure, juvenile arthritis, lupus, inflammatory bowel disease, and hypertension, as well as psychiatric disorders such as schizophrenia and bipolar disorder (Source: *Journal of Laboratory and Clinical Medicine,* Vol. 147(3):126-32, 2006).

The rapidly growing body of evidence demonstrates the potential for using peripheral blood as a surrogate material for traditional tissue specimens and biopsies used for prognosis and diagnosis. Blood provides significant advantages for this purpose, being readily available in large quantities with minimally invasive techniques. In addition, circulating blood cells have unique characteristics that make them a potential new tool for diagnostics and screening applications: (1) a large proportion of the genes encoded in the human genome have detectable levels of transcripts in circulating blood cells; (2) circulating blood cells come into contact with every cell in the human body and provide an active defense against injury; and (3) macro- and micro-environment changes affect gene expression in blood cells. Therefore, circulating blood cells may provide information as to the health or disease of any particular tissue by the change of gene expression pattern (Source: *Journal of Laboratory and Clinical Medicine,* Vol. 147(3):126-32, 2006).

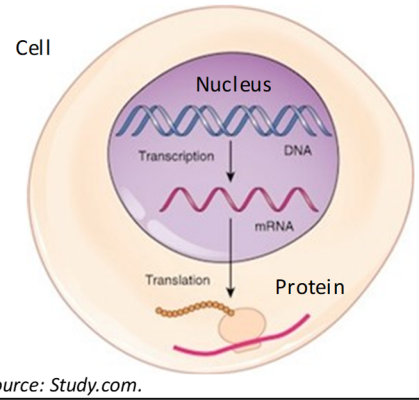
ColonSentry®, the Company's diagnostic test for colorectal cancer, specifically measures gene expression of seven unique mRNA biomarkers in whole blood capable of differentiating patients with cancer from healthy patients. In particular, the Company's technology uses subtle changes in a person's mRNA that occur due to cancer and that can be detected to identify the disease in its earlier stages.

Messenger RNA (mRNA)

Most people think of cancer as changes, or mutations, in the sequence of DNA that lead to uncontrolled cell division. However, in between DNA and proteins there is another layer of information called messenger RNA (mRNA). Changes in mRNA expression can be measured in blood and serve as specific early indicators for cancer and other diseases.

DNA is the genetic blueprint for life. The information in DNA is encoded in some 3 billion nucleotide "letters." Blocks of these letters—genes—are used to make particular proteins involved in every bodily function. But DNA lives in the nucleus of a cell, while proteins are made in the surrounding **cytoplasm**. To bridge this gap, a cell must first make an RNA copy of a gene's DNA. This RNA copy, called messenger RNA, is then transported out of the nucleus. It is this mRNA copy that cells read and translate into a protein (Figure 12).

Figure 12
mRNA



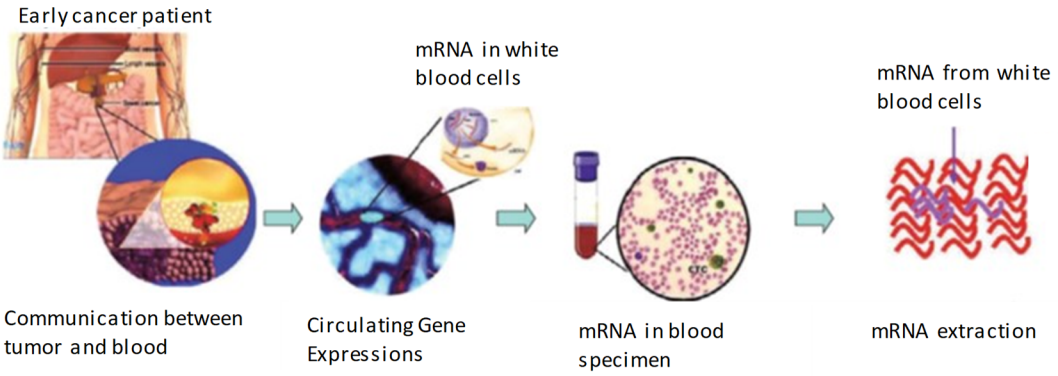
Source: Study.com.

Usually, the mRNA copy is a bit shorter than its DNA precursor, as it includes the useful pieces of information in DNA, called exons, and leave out blocks of unnecessary sequences, called introns. After the introns are removed, the remaining exons are spliced together, not unlike splicing together pieces of film and leaving some on the cutting room floor. If the mRNA copy does not include all of the exons in a gene or is cut short, then the protein made from that mRNA will also be truncated and may not function properly.

Alternative splicing can change the structure of mRNA by inclusion or skipping of exons, and this may alter the functionality, stability, or binding properties of encoded proteins and thereby contribute to human diseases such as cancer. Researchers have found that many of the alternative spliced mRNAs in cancer cells produce these truncated tumor-suppressor proteins, eliminating their cancer fighting abilities (Source: Memorial Sloan Kettering Cancer Center's *In a Twist, Scientists Find Cancer Drivers Hiding in RNA, Not DNA*, 2018).

The altered splicing mechanisms in cancer leads to cancer-specific cell expressions different from those occurring in healthy individuals. Cancer-specific splice variants are of significant interest as they can be used as cancer detecting biomarkers. In order to develop a reliable technique for the use of mRNA in cancer screening applications, as seen in Figure 13, it is necessary to identify the cancer-related mRNA markers suitable for cancer detection (Source: *Genomic Medicine, Biomarkers, and Health Sciences*, Vol. 3(1):9−16, 2011).

Figure 13
mRNA EXTRACTION PROCESS



Source: Genomic Medicine, Biomarkers, and Health Sciences.

This principle is the driving force behind the Sentinel Principle®'s ability to detect cancer. It is also what gives the proprietary technology platform its flexibility and wide application. By researching different disease areas, StageZero's scientists can generate specific combinations of biomarkers for numerous medical conditions, including many cancers as well as uses beyond oncology. This enables StageZero to focus on diseases with the greatest unmet need and largest opportunities to improve care. The Sentinel Principle® platform was the driving force behind the development of the Company's flagship product, ColonSentry®, a blood-based test for assessing an individual's current risk of having CRC. In addition, StageZero offers early cancer diagnostics and risk stratification solutions for the most prevalent cancers: *Early*CDT®-Lung (lung cancer); Prostate Health Index (prostate cancer); and BreastSentry™ (breast cancer).

COLONSENTRY®

ColonSentry® is a proprietary liquid biopsy test that uses advanced gene expression technology for the early identification of colorectal cancer (CRC). The ColonSentry® test assesses an individual's current risk, or probability, of having CRC through a convenient and revolutionary blood test. Initially developed in 2008 from a clinical study involving approximately 10,000 subjects in North America, ColonSentry® was broadly commercialized in 2014 and has been administered to over 100,000 patients throughout the U.S.

Colorectal cancer is the third most frequently diagnosed cancer in men and women in the U.S. and carries an overall population lifetime risk of about 4%. Despite being among the most preventable of neoplasms and surgically curable in early stages, CRC remains the second leading cause of cancer death in the western world. In the U.S., over 147,950 people were diagnosed with CRC in 2020 and some 53,200 died of the disease (Source: *CA: a Cancer Journal for Clinicians*, Cancer Statistics 2020).

Early diagnosis of CRC is critically related to patient survival. Localized cancers have an excellent 5-year survival prognosis (90%), regional stage patients have a 5-year survival rate about 71%, with only 14% of patients with late stage disease surviving 5 years. These numbers make CRC suitable for a screening program, and health authorities have long promoted screening for CRC in average-risk adults, beginning at the age of 50 years (Source: Cancer.org). Despite repeated recommendations and awareness campaigns, people have resisted CRC screening. Although 90% of respondents in studies express high interest in cancer screening in general and CRC screening in particular, screening compliance remains low. Only about 61.9% of age-eligible U.S. patients are current with recommended fecal or endoscopic-based tests (Source: JAMA Oncology and Preventing Chronic Diseases).

ColonSentry® Development

ColonSentry® is a convenient blood-based CRC risk prediction test for assessing the potential of CRC in average risk individuals. The liquid biopsy test uses a seven-gene biomarker panel to stratify average-risk patients into subgroups according to their current relative risk of having CRC. Unlike other screening tests, ColonSentry® is not a "yes or no test," but provides an actual risk score for a patient.

Risk is determined by measuring the levels of seven biomarker genes in a whole blood sample. mRNA gene expression levels of six overexpressed genes—ANXA3, CLEC4D, LMNB1, PRRG4, TNFAIP6, and VNN1—are each paired with the expression level of an underexpressed gene, IL2RB, to create a gene signature by which patients can be stratified for CRC risk. This seven-gene biomarker combination enabled development of a scale providing enriched information about an individual's risk for having CRC. As a blood test, it addresses one of the greatest challenges currently limiting CRC screening effectiveness: lack of compliance. Additionally, by identifying patients with enhanced CRC risk, this approach can help healthcare providers assess the need for increased monitoring. Figure 14 (page 25) list the functions of the seven genes that contribute to the ColonSentry® molecular signature.

Figure 14

FUNCTIONS OF COLONSENTRY GENES

IL2RB	The reference gene, encodes the beta subunit of the interleukin 2 (IL-2) receptor. Specific binding of the T-cell-derived cytokine IL-2 to this receptor is critical for the growth, proliferation, and differentiation of naïve T cells into effector T cells, which are able to target and destroy cancer cells.
ANXA3	Encodes annexin A3, a member of the annexin protein family. Annexins play a role in the regulation of cellular growth and intracellular signaling.
CLEC4D	Codes for a member of the C-type lectin protein superfamily. Proteins with C-type lectin domains can bind carbohydrates and have diverse functions including cell-cell adhesion, immune response to pathogens, and apoptosis.
LMNB1	Encodes the protein lamin-B1. The cellular lamina, a 2-dimensional protein matrix located adjacent to the inner nuclear membrane, is thought to be involved in nuclear stability, chromatin structure, and gene expression.
PRRG4	Encodes one member of a family of proline-rich γ-carboxyglutamic acid (PRRG) proteins. Recent studies have identified a role for PRRG4 in cancer, allergy, and neurological disorders.
TNFAIP6	Encodes the tumor necrosis factor-inducible gene 6 protein, also known as TSG-6, which is involved in cell-cell and cellmatrix interactions during inflammation and tumorigenesis.
VNN1 (Vanin-1)	Encodes pantetheinase, an enzyme thought to be involved in regulation of the immune response to oxidative stress.30 VNN1-AB has been shown to be a potential biomarker for colorectal cancer.

Source: StageZero Life Sciences, Ltd.

Clinical validation results were published in 2009 in the International Journal of Cancer. In this study, a set consisting of 112 CRC cases and 120 control cases was first used to identify the best combination of genes, generating the aforementioned biomarker panel. Researchers then developed a risk scale to assess the likelihood of an individual having CRC using a logistic **regression-based algorithm** derived from the expression levels of these seven genes. This test demonstrated the ability of its seven-gene biomarker panel to detect lesions with 64% specificity, 82% sensitivity, and 73% accuracy values. The predictive capability of the seven-gene panel was then validated on a blind test set consisting of 202 CRC cases and 208 controls, resulting in 70% specificity, 72% sensitivity, and 71% accuracy (Source*: International Journal of Cancer*, Vol. 126: 1177–1186, 2010).

Further tests assessed ColonSentry®'s ability to detect both left-sided and right-sided colon lesions. Colonoscopy is widely regarded as the gold standard for CRC detection. However, studies have found that although colonoscopy's effectiveness is high for lesions on the left side, the technology has poor tumor detection for right-sided lesions. During the test, the seven-gene biomarker panel detected right-sided CRC lesions across all cancer stages with a sensitivity that was at least equal to that for left-sided lesions. The panel detected left-sided (74%, 154/208) and right-sided (85%, 92/108) lesions with an overall sensitivity of 78% (215/316) at a specificity of 66% (215/328). Treatable cancer (stages I to III) was detected with left-sided lesion sensitivity of 76% and right-sided sensitivity of 84% (Source: *Journal of Experimental & Clinical Cancer Research*, Vol. 32 (44), 2013).

ColonSentry® test was further validated in a Malaysian case-control study. The independent Malaysian study validated the seven-gene panel using blood samples from 99 CRC patients and 111 controls (Source: *Journal of Experimental & Clinical Cancer Research*, Vol. 29:128, 2010). ColonSentry's performance was evaluated on 100,000 patients to assess whether quality control limits and stability was maintained over multiple years (Source*: International Journal of Disease Markers*, Vol. 2019; Issue 01, 2019). Figure 15 provides an overview of ColonSentry®'s validation findings.

Figure 15

COLONSENTRY® VALIDATION

Validated	Utilized	Detects	Finds
10,000 patients study in North America	100,000+ test performed in the U.S.	Cancers in stages 1-4	Left and Right sided colorectal lesions

Source: StageZero Life Sciences, Ltd.

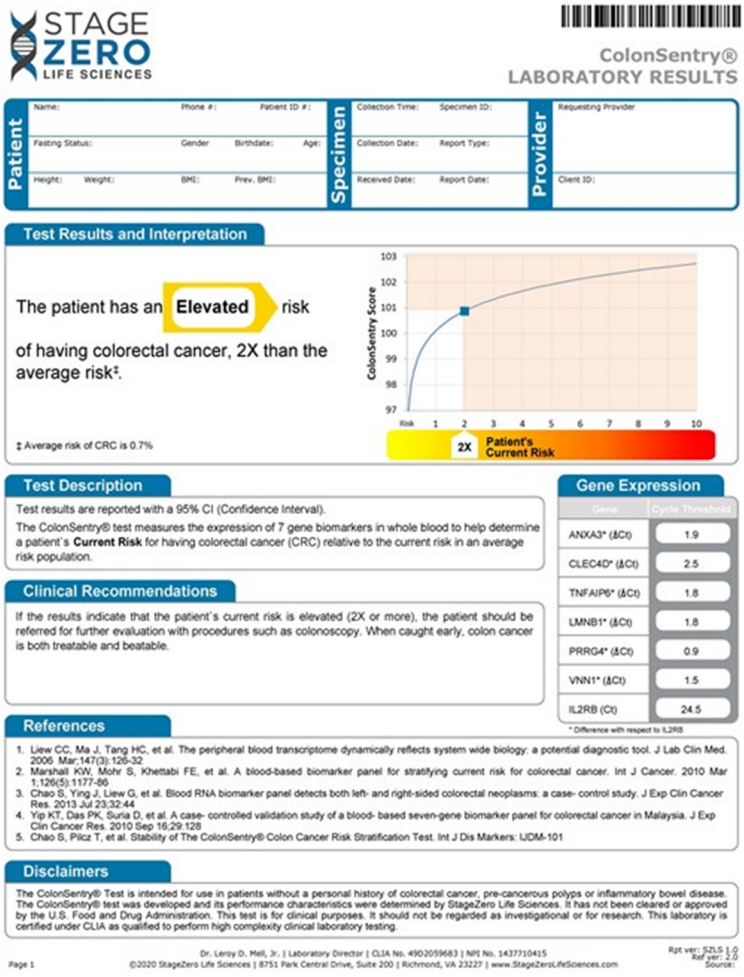
The ColonSentry® Process

ColonSentry® is a patient-friendly, blood-based test that can be easily incorporated into a routine physical examination which can be performed at a patient's annual exam. The test acts as a convenient companion diagnostic and a pre-screening alert, ultimately leading to enhanced CRC screening effectiveness.

Following the American Cancer Society's recommendation that people at average risk of colorectal cancer start regular screening at age 45, patients may be candidates for the ColonSentry® Test if they meet the following criteria: (1) age 45 or older and at average risk for colorectal cancer; (2) are without symptoms, such as bleeding, abdominal pain, or change in bowel habits; and (3) have not had a colonoscopy or stool-based screening test.

Figure 16

COLONSENTRY REPORT



Source: StageZero Life Sciences, Ltd.

The implementation of ColonSentry® provides the physician and patient with an easy-to-understand report (Figure 16, page 26). The sample processing takes place on the Company's CLIA-accredited laboratory in Richmond, Virginia. If the ColonSentry® score is elevated, there is an increased probability the patient may have a CRC. Thus, patients with elevated ColonSentry® scores should be encouraged to have a colonoscopy. An added benefit of ColonSentry® is the fact that data accumulated through its clinical use indicates that patients with elevated ColonSentry® scores are more likely to move forward with a colonoscopy.

ColonSentry® can be incorporated into CRC decision making in several ways. A blood test would benefit patients who desire information about their CRC status but refuse screening due to their dislike of screening options. In particular, identification of increased CRC risk may facilitate colonoscopy decision-making for these patients who would otherwise refuse a colonoscopy. In addition, in healthcare systems with limited colonoscopy capacity, this approach could help prioritize patients at greatest current risk for CRC.

ColonSentry®'s Advantages

The clinical advantages of ColonSentry® are significant. First, ColonSentry® increases patients CRC screening compliance. Studies show that 80% to 95% of patients who refuse colonoscopies will comply with a blood test, in line with ColonSentry®'s 95% in-office compliance rate. Following a ColonSentry® test result, patients are two times more likely to comply with a colonoscopy. ColonSentry® can identify those elevated risk patients that have yet to comply with any form of CRC, motivating them to have a colonoscopy. ColonSentry® can also be used in elderly patients with an increased risk of complications from colonoscopy. New efforts to improve screening through risk stratification tools are essential for ensuring the 'unscreened' population gets screened, whether through colonoscopy or stool-based procedures. ColonSentry®, as a risk stratification test, helps primary care physicians facilitate the discussion about colon cancer screening with the eligible population who have refused to undergo other tests such as colonoscopy, Cologuard, or FIT.

In addition, it may also be considered for patients who are younger than the currently recommended screening age, but who have CRC risk factors, such as diabetes, obesity, or history of smoking. Screening of such individuals could detect a substantial number of CRCs; of the 588,869 CRC diagnoses made between 1998 and 2007, 10.9% (or over 64,000 cases) occurred in people under the age of 50 (Source: *Archives of Internal Medicine*, Vol. 172(3):287-289, 2012). Studies indicate that among individuals in this age group who undergo colonoscopy screening, roughly 21.1% have abnormal findings, including hyperplastic polyps, tubular adenomas, and advanced neoplasms (Source: *New England Journal of Medicine*, Vol. 346(23):1781-1785, 2002).

Another advantage of ColonSentry® is the fact that the test increases the effectiveness of current screening methods and improves patients' outcomes. ColonSentry® has the ability to detect both left-sided and right-sided lesions. This information can increase the effectiveness of CRC screening by revealing the potential presence of neoplasms in advance of the procedure. According to the Company, performing the ColonSentry® test in advance of a colonoscopy results in the detection of 2.1 to 4.7 times more CRC lesions. Furthermore, ColonSentry® may help physicians monitor for so-called interval cancers. StageZero's ColonSentry® can be used to monitor colonoscopy-compliant patients for interval cancers in the time between the scheduled colonoscopies (normally 10 years).

ColonSentry® further provides financial benefits to both the consumer and health plans, facilitating its uptake in the industry. ColonSentry® can reduce healthcare costs by more than 20% through early intervention. If alternative (and more expensive) screening test are performed, such as Computed tomography (CT), colonography (virtual colonoscopy), or Cologuard, and a positive result is found, the patient is no longer preventative screening but now is diagnostic when referred for colonoscopy (meaning that the patient has a 20% financial responsibility for the colonoscopy, facility, anesthesia, pathology, etc.). This compares to ColonSentry®, which is a risk stratification test that preserves the patient as being seen for a preventive screening service, without financial responsibility, when referred for colonoscopy.

According to the Company, ColonSentry® has demonstrated a negative predictive value (the probability that subjects with a negative screening test do not have the disease) of 99.6%, an important measure for cancer screening test, which means that the chances of missing colorectal cancer is less than 0.04 percent (Source: *International Journal of Cancer*, Vol. 126:1177-1186, 2009).

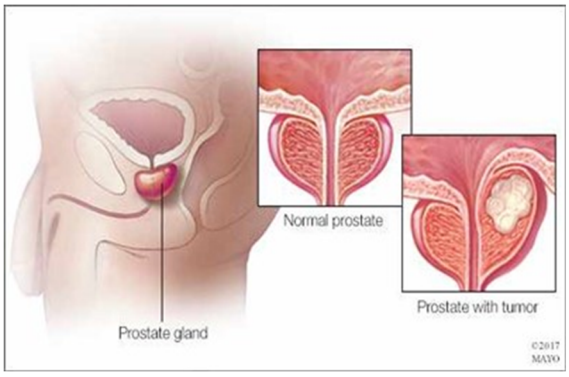
PROSTATE HEALTH INDEX (*phi*)

The Prostate Health Index (*phi*) is a convenient blood test that uses three different PSA markers (PSA, free PSA, and pro2 PSA) as part of a sophisticated calculation to more reliably determine the probability of prostate cancer in patients with elevated PSA levels. *Phi* helps physicians distinguish prostate cancer from benign conditions and is three times more specific in detecting prostate cancer than the PSA test. Using *phi* to stratify patients with elevated PSA may reduce exposure to complications of unnecessary prostate biopsy including pain, bleeding, and infection.

Developed by Beckman Coulter and widely used in Europe under CE mark approval, the *phi* index was granted approval by the U.S. Food and Drug Administration (FDA) in June 2012 for determining the probability that prostate cancer is present and is included in the National Comprehensive Cancer Network (NCCN) Guideline for Prostate Cancer Early Detection as a blood test to improve specificity for prostate cancer detection. The Company executed an agreement with Beckman Coulter in 2014 that allows it to include the *phi* test in its portfolio of cancer screening offerings.

Prostate Cancer Background

Figure 17
PROSTATE CANCER



Source: Mayo Clinic.

Prostate cancer (Figure 17) is a leading cause of cancer mortality in men. It is estimated that 191,930 new cases of prostate cancer were diagnosed in 2020, making it the most common cancer type among men, representing 20% of total cancer cases. Furthermore, 33,330 men died of prostate cancer, the second leading cause of cancer death in U.S. men (Source: *CA: a Cancer Journal for Clinicians*, Cancer Statistics 2020).

Early detection of the disease is key to prognosis. Five-year survival for prostate-cancer patients with early stage disease is nearly 100%, and survival rates remain high at 10 years. However, that figure decreases to 31% for 5-year survival if the cancer is detected at a late stage (Source: American Cancer Society's *Cancer Facts & Figures 2020*).

Despite this, only 35.8% of men older than 50 reported having a PSA test in the past year (Source: *Preventing Chronic Diseases'* Volume 15 (E97), 2018). In addition, while the PSA test is currently the most widely used screening test for prostate cancer, it is generally recognized that the PSA test lacks the specificity for accurate prostate cancer detection, with results that often indicate the possibility of prostate cancer when none is present. The PSA test is based on the fact that men with higher levels of PSA are more likely to have prostate cancer. However, higher levels of PSA can also be caused by a benign enlargement or inflammation of the prostate, leading to many false-positives and ultimately unnecessary, invasive biopsies with an increased potential for patient harm.

PSA Test

PSA, a protein produced by prostate epithelial cells, is a commonly used serum marker for prostate cancer as cancer-induced changes can lead to increased leakage of PSA into the bloodstream. However, total PSA tests alone lack the specificity for accurate prostate cancer detection because PSA leakage and resultant increases in serum PSA can also be caused by benign conditions such as prostatitis and benign prostatic hyperplasia (BPH). Although PSA testing was approved by the FDA using a 4.0 ng/mL cutoff for recommending prostate biopsy, the low specificity at PSA level under 10.0 ng/mL has created a diagnostic gray zone in which prostate cancer is found on biopsy in only 25% of patients with PSA in the range between 2 µ g/L and 10 µ g/L. This is important since most prostate cancers are treatable at PSA levels under 10.0 ng/mL, but levels above that cutoff often indicate advanced disease (Source: *Journal of Urology*, Vol. 185(5): 1650–1655, 2011).

The lack of specificity of PSA tests results in unnecessary biopsies due to false positive results. Prostate biopsy may be associated with discomfort, anxiety, and financial costs. Minor complications occur frequently, and major complications are possible. While there is persistent debate over the risk-to-benefit ratio of PSA-based screening for prostate cancer, there is general agreement about the need for new markers that improve the accurate detection of prostate cancer and reduce the incidence of unnecessary biopsies.

Free PSA and p2PSA

To preserve the benefits of screening and early detection and to reduce the harm from unnecessary biopsies, there has been great progress into alternate ways of using the PSA test. In the early 1990s, several studies showed that the percentage of PSA circulating in the unbound form (known as free PSA [fPSA]) indicated a greater likelihood that the PSA elevation was from benign conditions rather than prostate cancer (Source: Therapeutic Advancements in Urology, Vol. 6(2) 74–77, 2014). Although the use of fPSA significantly improves the discrimination of prostate cancer from benign conditions, fPSA-based screening still results in a high number of unnecessary prostate biopsies. More recently, fPSA has been found to include three distinct molecular forms (BPSA, iPSA, and proPSA) and while BPSA and iPSA are associated with benign tissue, proPSA is associated with cancer and can further increase the specificity for prostate cancer tests.

Initial clinical studies demonstrated that proPSA may be a useful marker for the detection of prostate cancer. In particular, the [-2] truncated form of proPSA (p2PSA), has become commercially available, with improved performance over either total or fPSA for prostate cancer detection on biopsy (Source: *Therapeutic Advancements in Urology*, Vol. 6(2) 74–77, 2014). In clinical studies of patients with PSA ranging from 2.0–10.0 ng/mL, the proPSA-to-fPSA ratio (%proPSA) yielded a higher specificity than %fPSA. Results from a separate multi-site study also supported the role of p2PSA, in combination with PSA and fPSA, in reducing unnecessary biopsies (Source: *Journal of Urology*, Vol. 185(5): 1650–1655, 2011).

Prostate Health Index (*phi*)

Phi is a new formula that combines all three different PSA markers (PSA, fPSA, and p2PSA) as part of a sophisticated algorithm to more reliably determine the probability of cancer in patients with elevated PSA levels. The *phi* test is designed to improve upon the specificity of PSA and %fPSA for prostate cancer detection, and is calculated using the following formula:

phi = (p2PSA/fPSA) × (√total PSA)

Higher *phi* values are associated with increased probability of prostate cancer, and with more aggressive disease. This risk score, along with factors such as overall health and life expectancy, can help clinicians and patients determine whether a man would benefit from prostate biopsy. *Phi* reduces unnecessary biopsies by 30% percent for men with PSA values between 2-10 ng/mL. The test also preferentially detects more aggressive, potentially life-threatening cancers that most agree require treatment (Source: Mayo Clinic).

Clinical Validation

In 2011, a multi-center pivotal clinical trial sponsored by Beckman Coulter, the creator of *phi*, demonstrated that *phi* significantly enhanced specificity for prostate cancer detection compared to PSA and %fPSA for men over age 50 with PSA in the 2-10 ng/mL range. The study enrolled 892 men between 50 and 84 years of age with total PSA levels in the diagnostic "gray zone" of 2 to 10 ng/ml and normal digital rectal examination (DRE) who were undergoing prostate biopsy. Researchers examined the relationship of serum PSA, %fPSA and phi to the biopsy results. The study showed that the diagnostic accuracy of *phi* (~70%) was significantly greater than those for PSA, fPSA, and %fPSA (~53%, 62%, and 65%, respectively). Higher *phi* values were associated with increased probability of prostate cancer being present, and with more aggressive disease, with mean *phi* scores of 34 and 49 for men with negative and positive biopsies, respectively. For example, men with *phi* above 55 had a greater than 52% probability of prostate cancer and a 4.7-fold increased risk of positive biopsy (Figure 18, page 30).

Furthermore, the specificity for *phi* was higher than %fPSA and PSA at all pre-specified sensitivities, as seen in Figure 19. Moreover, *phi*—unlike PSA and fPSA—was not found to be associated with age or prostate volume. The marked improvement in specificity of *phi* represents a substantial advance in testing to distinguish prostate cancer from benign conditions (Source: *Journal of Urology*, Vol. 185(5): 1650–1655, 2011).

Figure 18
RISK OF PROSTATE CANCER PER *phi* SCORE

***phi* Score**	**0-24**	**25-34**	**35-54**	**>55**
Pr of Pca in biopsy	11.0%	18.1%	32.7%	52.1%
Risk of Pca detection		x1.6	x3	x4.7

Source: Journal of Urology.

Figure 19
phi SPECIFICITY RESULTS

sensitivity	**PSA**	***phi***
95	6.5	16
90	18	26
85	28	39
80	37	45

Source: Journal of Urology.

Multiple clinical trials have since corroborated the findings of the original Beckman Coulter-sponsored study. A recent systematic review and meta-analysis of studies totaling nearly 3,000 patients concluded that *phi* significantly improves the accuracy of prostate cancer detection in comparison with PSA or %fPSA, particularly in patients with PSA between 2-10 ng/ mL. The available data shows that *phi* may be useful in the detection of prostate cancer, reducing the number of negative biopsies and improving those results obtained with %fPSA and total PSA. Recently published data concerning cost-effectiveness of these tests also suggests a positive budget impact of *phi*'s generalized implementation in the management of prostate cancer. Data also showed a link between high *phi* values and the aggressiveness of the tumor (Source: *Clinical Chemistry and Laboratory Medicine*, Vol. 51(4):729-739, 2013).

Several large international studies have not only confirmed the fact that *phi* outperforms its individual components for the prediction of overall and high-grade prostate cancer on biopsy, but have also shown *phi*'s ability to predict the likelihood of progression during active surveillance, providing another noninvasive modality to potentially select and monitor the patient population. Among those, the PRO-PSA Multicentric European Study of 646 European men undergoing prostate biopsy for a PSA of 2 to 10 ng/ml or suspicious DRE showed that p2PSA and *phi* significantly improved the prediction of biopsy outcome over total and free PSA (with *phi* missing the fewest high-grade tumors), with their use reducing the number of unnecessary biopsies by ≥15%. (Source: *Therapeutic Advancements in Urology*, Vol. 6(2) 74–77, 2014).

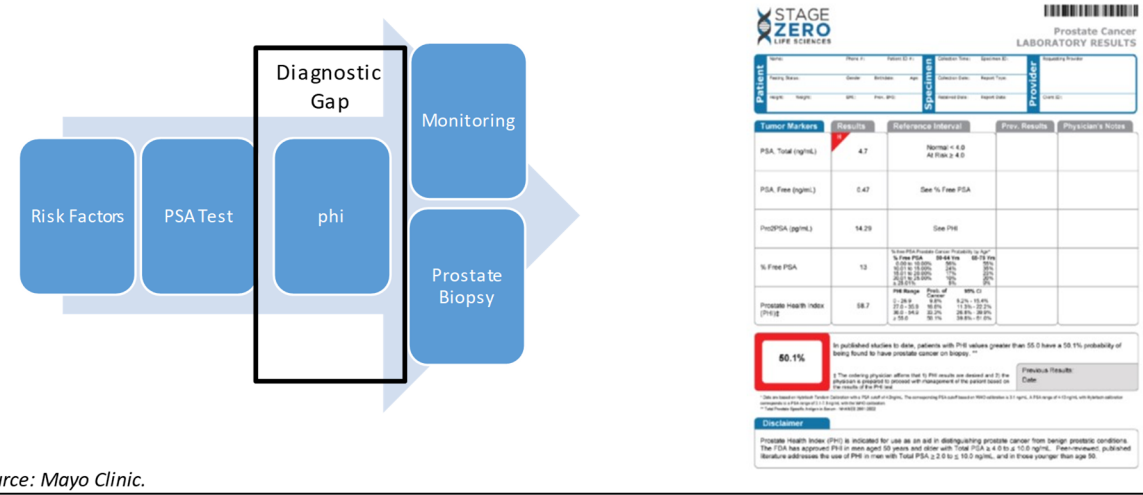
***PHI* Process**

The Prostate Health Index (*phi*) is indicated for use as an aid in distinguishing prostate cancer from benign prostatic conditions in men aged 50 years and older with elevated PSA between 4 ng/ml and 10ng/ml. The test is intended to fill the diagnostic gap between PSA tests and biopsies, aiding in the decision to perform the procedure and avoiding unnecessary biopsies, as seen in Figure 20 (page 31).

The percentage likelihood of prostate cancer being found on biopsy is derived from the *phi* value, with higher *phi* scores associated with an increased probability of prostate cancer on biopsy and is color coded; low probability (grey); medium probability (yellow); and high probability (red) (Figure 20). Patients whose test results indicate elevated prostate cancer risk may choose to undergo prostate biopsy or, instead, be closely monitored for signs of disease progression (active surveillance). If the *phi* score is medium or low, active surveillance with a repeat phi at a subsequent time may be an option to guide patient care. In particular, a *phi* score of less than 27 indicates a higher likelihood of a benign condition, while a *phi* score that is greater than 35 indicates the increased possibility of prostate cancer. A *phi* score above 55 indicates a more than 1 in 2 chance (52.1%) of prostate cancer.

Figure 20

PROSTATE CANCER DIAGNOSTIC GAP



Source: Mayo Clinic.

***EARLY*CDT®-LUNG**

*Early*CDT®-Lung is a sophisticated blood test that, in combination with Low Dose Lung CT, aids physicians in the early detection of lung cancer. *Early*CDT®-Lung measures a panel of seven autoantibodies associated with small cell and non-small cell lung cancers and can detect all types of lung cancers at every stage of the disease (I-IV) with high accuracy. StageZero licensed *Early*CDT®-Lung in January 2014 from Oncimmune Ltd, a UK-based company, for marketing, sale, and distribution of this test throughout the U.S. With the ability to include *Early*CDT®-Lung into their portfolio, the Company strengthens its focus on offering highly novel, blood-based tests that lead to early cancer diagnosis.

Lung cancer is the leading cause of cancer deaths among adults in the U.S., taking the lives of more people each year than colon, breast, and prostate cancers combined. Over 228,820 new cases of lung cancer are expected to be diagnosed in 2020, with 135,720 people dying of the disease.

Despite advances in surgical techniques, radiation therapy, and systemic therapy, the outlook for patients with lung cancer has improved more slowly than many other cancers over the last 50 years. Lung cancer has a high mortality rate, with localized stage patients displaying a 57% 5-year survival prognosis. However, when the disease is diagnosed in the distant stage, the 5-year survival rate is only 5%. Thus, early detection of lung cancer is key. Despite this, 57% of lung cancers are found in the late stage, and 79% of them are found in the distant or regional phase. This is due to two key factors: (1) lung cancer may be asymptomatic in its early stages; and (2) compliance of screening recommendations is very low, with only 3.9% of high-risk smokers in the U.S. receiving their recommended LDCT screening (Sources: American Cancer Society's *Cancer Facts & Figures,* 2020 and JAMA *Oncology*, Vol. 3(9):1278-1281, 2017).

Currently, CT scan is the recommended screening method for lung cancer. CT scans are leading to a significant increase in the number of patients being diagnosed with lung nodules. However, lung nodules—small masses of tissue in the lung, which appear as round, white shadows on a chest X-ray or CT scan—are common. Over 95% of lung nodules on CT scans are false positives, i.e. not cancer. Given the large number of benign nodules detected by computed tomography, an adjunctive test capable of distinguishing malignant from benign nodules would benefit practitioners. *Early*CDT®-Lung can be used in conjunction with CT scanning to rule-in and assess the risk of cancer in patients at increased risk, especially those in whom indeterminate pulmonary nodules are found.

EarlyCDT®-Lung Background

During tumorigenesis, normal cells produce a number of novel abnormally expressed or mutated proteins (autoantigens), which are recognized by the immune system as 'non-self' and elicit the production of antibodies against them (autoantibodies). Autoantibodies arise in the early stages of lung cancer development, can also be present at later stages, and exist in sufficient quantity and size to be measurable in blood even when the tumor may be small and/or localized. Elevated levels of autoantibodies beyond predetermined cutoffs could be indicative of disease.

*Early*CDT®-Lung is an enzyme-linked immunosorbent assay (ELISA) that measures blood levels of seven lung cancer associated autoantibodies (CAGE, GBU4-5, p53, NY-ESO- 1, SOX-2, MAGE A4, HuD). Elevation of any one of the seven autoantibodies above a predetermined cut-off value suggests that a tumor may be present, necessitating a follow-up test(s) (e.g., CT). Even if the autoantibody levels all lie below the cutoff, the patient is still considered high risk because of associated risk factors, such as smoking, whereby monitoring via follow-up testing with *Early*CDT®-Lung is recommended, along with adherence to current lung cancer screening recommendations by the US Preventive Services Task Force (USPSTF).

*Early*CDT®-Lung significantly aids the assessment of malignancy risk in pulmonary nodules. *Early*CDT®-Lung can help aid early lung cancer detection, leading to earlier intervention and better patient outcomes. In a cohort of 296 patients with a pulmonary nodule(s), a positive *Early*CDT®-Lung test was associated with a more than two-fold increase in risk of lung cancer for nodules 4 to <20 mm (n=196) (Source: *Journal of Thoracic Oncology*, Vol. 12(3):578-584, 2017).

Clinical Validation

The effectiveness of *Early*CDT®-Lung has been validated by an extensive number of trials and studies, including over 25 peer-reviewed clinical publications and more than 60 peer-reviewed oral and poster presentations at key conferences. In all, there are over 120,000 patient samples examined and 12 million data points analyzed to validate the technical and clinical performance of *Early*CDT®-Lung in early lung cancer diagnosis. The test consistently identifies lung cancer with 92% accuracy (compared with 50% for CT) with a sensitivity (true positive rate) of ~40% for all stages and types (small cell and non-small cell) of lung tumors and a specificity (true negative rate) of ~93% for all cohorts (Source: *Journal of Cancer Therapy*, Vol. 8:506-517, 2017).

The performance characteristics of the *Early*CDT®-Lung test were initially validated in the commercial setting by an audit of clinical outcomes for the first 1,613 patients deemed at high risk for lung cancer by their physician, who had a valid *Early*CDT®-Lung and unknown nodule status. In the study, *Early*CDT®-Lung was found to be a valuable complementary tool to CT for detecting early lung cancer. A positive result on the *Early*CDT®-Lung test was associated with a 5.4-fold increase in incidence of lung cancer compared to a negative test (Source: *Lung Cancer*, Vol. 83 51–55, 2014).

In a more recent study, data published in 2017 by Oncimmune in the *Journal of Thoracic Oncology* demonstrated the effectiveness of the *Early*CDT®-Lung test in discriminating between benign versus malignant lung nodules. A positive autoantibody test result reflected a significant increased risk for malignancy in lung nodules 4 to 20 mm in diameter. In 296 eligible patients after exclusions, a positive test result represented greater than a two-fold increased relative risk for developing lung cancer versus a negative test result (Source: *Journal of Thoracic Oncology*, Vol. 12(3):578-584, 2017).

*Early*CDT®-Lung is currently being evaluated in the largest randomized trial for the early detection of lung cancer through the National Health Service (NHS) Scotland. The trial is evaluating the test in 12,000 high-risk patients. Patients who had a positive result from the *Early*CDT®-Lung test and were sent for further CT follow-up. Preliminary data has shown that the *Early*CDT®-Lung test can detect lung cancer as much as two or more years before it may be seen via LDCT. A raised risk score, followed up aggressively for two years, demonstrated a sensitivity of 81%, while maintaining a specificity of 91%. This contrasts with the validation studies where, with only a six month follow up, sensitivity was 40%. The difference is in aggressive follow-up for a significant enough time to allow LDCT to detect the malignant nodule, as LDCT typically will not differentiate well for nodules below a range of 2-4 mm.

BREASTSENTRY™

In October 2014, StageZero in-licensed two blood-based biomarker assays—proneurotensin (pro-NT) and proenkephalin (pro-ENK)—intended to aid physicians in identifying those women who are at risk for developing breast cancer. These assays were developed by sphingotec GmbH, known for the discovery and development of biomarker assays. The Company used these two assays for the creation of BreastSentry™, a blood test and algorithm that can help determine if a female patient should be referred for advanced breast diagnostic procedures. BreastSentry™ measures the levels of the biomarkers, pro-NT and pro-ENK, which are highly predictive of a woman's risk for developing breast cancer. Elevated levels of pro-NT and decreased levels of pro-ENK are risk factors for developing breast cancer.

Breast cancer is the most frequently diagnosed cancer and the second leading cause of cancer death among women in the U.S. An estimated 276,480 women are expected to be diagnosed with breast cancer in 2020, with 42,170 dying of the disease (Source: American Cancer Society's *Cancer Facts & Figures, 2020*).

Early detection is key in breast cancers prognosis. Five-year survival for breast cancer patients with early stage disease is 99%, and survival rates remain high at 10 years. However, that figure decreases to 27% 5-year survival if the cancer is detected at a late stage (Source: American Cancer Society's *Cancer Facts & Figures, 2020*). Despite breast cancer screening being more common than those for other types of cancers, with 71.7% of women aged 50 to 74 reporting a recent mammogram, over a third of cases are still diagnosed in the advance stages of the disease.

This is due to the shortcomings of mammograms. An estimated 20% of breast cancers are missed at least once by mammography, especially if the patient has dense breasts, which affects approximately 50% of women. In addition, mammograms result in a high number of false positives, with approximately half of the women getting annual mammograms over a 10-year period expected to have a false-positive finding (Source: American Cancer Society's *Limitations of Mammograms*).

BreastSentry™ Background

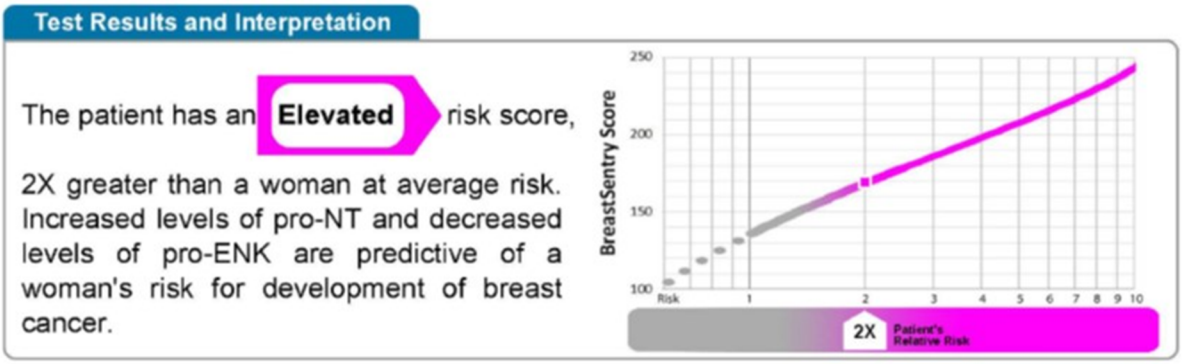
BreastSentry™ measures the fasting plasma levels of pro-NT and pro-ENK, two biomarkers which are highly predictive of a woman's risk for developing breast cancer. Various longitudinal studies have shown that elevated levels of pro-NT and decreased levels of pro-ENK are strong, independent risk factors for the development of breast cancer. The combined test levels have been incorporated into a sophisticated algorithm in order to provide an additional level of personal data to create an enriched, personalized score. BreastSentry™ is used to determine a woman's risk for developing breast cancer relative to the risk in an average risk population.

Many breast cancer cases are not due to genetic inheritance and, unlike other blood tests on the market that look for genetic indicators for the possibility to develop breast cancer, pro-NT and pro-ENK are biomarkers that when measured in a convenient blood test, indicate the current level of a woman's risk for breast cancer.

The BreastSentry test is indicated for use in average risk women, defined as women without any of the following risk factors: (1) personal history of breast cancer; (2) confirmed or suspected genetic mutation known to increase risk of breast cancer (e.g., BRCA); (3) history of previous radiotherapy to the chest at a young age; and (4) history of kidney disease. The BreastSentry test provides patients with their risk of developing breast cancer in the future. The test provides a risk score for each patient, as seen in Figure 21 (page 34). Physicians can monitor patients with an elevated risk score more closely, prescribe additional screening and/or encourage their patients to make lifestyle changes to reduce their risk of breast cancer. Women with elevated BreastSentry™ scores, especially women over the age of 40 with dense breast tissue, may need to be referred for advanced imaging tests, such as breast MRI, in addition to a screening mammogram

Figure 21

BREASTSENTRY™ REPORT



Source: StageZero Life Sciences, Ltd.

BreastSentry™ Validation

Two large Swedish general population longitudinal studies were used to validate the BreastSentry™ test. The Malmö Diet and Cancer study (MDC); the Malmö Preventive Project (MPP) found a significant predictive relationship between individual pro-NT and pro-ENK biomarkers and the development of breast cancer. Results from the MDC study showed a highly significant relationship between the concentration of pro-NT in the blood and the risk of developing breast cancer; the MPP study confirmed these results.

The Malmö Diet and Cancer study is a 10-year prospective case-control study in 53,000 45-64-year-old men and women living in Malmö, the third largest city of Sweden. The main objective was to clarify whether a western diet was associated with certain forms of cancer. In addition, a biomarker program, utilizing the biological bank, was developed and aimed at finding predictors and/or precursors of cancer. The MDC study followed participants for a mean of approximately 15 years and a maximum of 18 years (Source: *Journal of Internal Medicine*, Vol. 233(1):45-51, 1993). The MPP, also conducted in Malmö, performed clinical examination, questionnaire, and blood sampling in 22,444 men and 10,902 women. The MPP study followed participants for a mean of approximately five years and a maximum of eight years (Source: Swedish National Data Service).

Utilizing the biological bank of the MDC study, researchers found a highly significant relationship between the concentration of pro-NT in the blood and the risk of developing breast cancer; the results showed that an increased pro-NT level demonstrated an almost threefold higher risk in developing breast cancer in the following 10-18 years. (Source: *JAMA*, Vol.308(14):1469-75, 2012). Analysis of the MPP biobank samples confirmed these results (Source: *Cancer Epidemiology*, *Biomarkers Prevention*, Vol.23(8):1672-6, 2014). Researchers also linked levels of pro-ENK to breast cancer incidence using the MDC study data, with low plasma concentration of pro-ENK associated with an increased risk of future breast cancer in middle-aged and postmenopausal women (Source: *Journal of Clinical Oncology*, Vol.33(24), 2015). It was also shown in these studies that biomarker-based risk prediction for the development of breast cancer was significantly improved by combining the measurements of both plasma pro-ENK and pro-NT (Source: *Cancer Research* Vol.73(24 Suppl), 2013). StageZero used the banked samples from the MPP and MDC studies in developing and validating the algorithm.

ARISTOTLE™

Utilizing its Sentinel Principle® technology, StageZero is developing Aristotle™, its next generation multi-cancer panel for the simultaneous screening of 10 cancers (colorectal, prostate, cervical, endometrial, breast, ovarian, liver, bladder, nasopharyngeal, and stomach cancer) from a single sample of blood, with high sensitivity and specificity for each cancer. The Company has conducted early validation studies for the technology and anticipates a 2021 time to market.

Aristotle™ has been built on the Company's proven and proprietary mRNA and Sentinel Principle® technology platform. This platform has been validated through the development of ColonSentry®, a blood test for the early detection of CRC (described on pages 24-27). Furthermore, the Company is planning to capitalize on the flexibility of its Sentinel Principle® technology platform and expand the applications of Aristotle™ beyond oncology to help in the diagnosis of disease states in gastroenterology, neurology, cardiology, autoimmune disease, heart disease, and psychiatric disorders. Figure 22 provides an overview of Aristotle™'s capabilities.

Figure 22

ARISTOTLE™ OVERVIEW

1 SAMPLE OF BLOOD	10 SPECIFIC CANCERS	HIGH SENSITIVITY AND SPECIFICTY	CAN FULLY DISCRIMINATE EACH CANCER
BUILT ON PROVEN PROPRIETARY TECHNOLOGY PLATFORM			

Source: StageZero Life Sciences, Ltd.

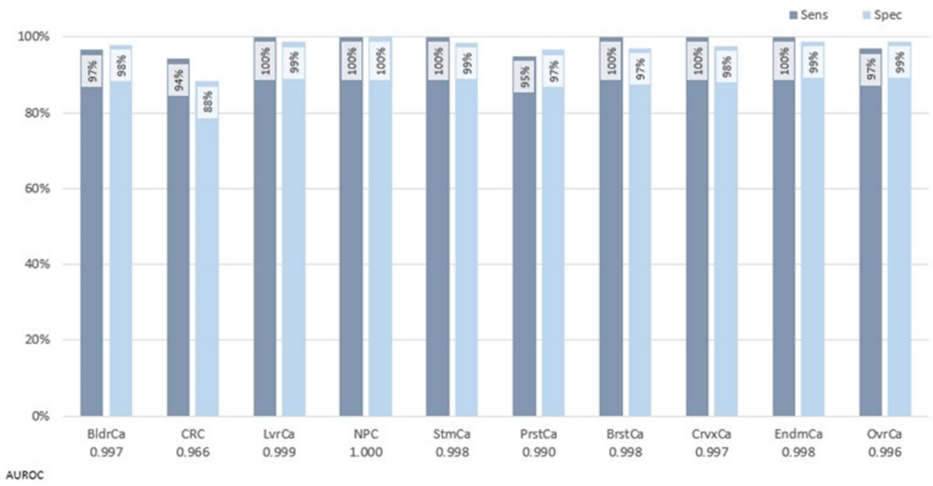
Aristotle™ Clinical Validation

The Sentinel Principle® posits that subtle changes that occur in cells due to injury or disease trigger detectable changes in gene expression in the blood. The multi-cancer panel platform, Aristotle™, has demonstrated to be able to identify sets of gene transcripts capable of classifying subjects as having a specific cancer with a high degree of sensitivity and specificity. Early validation of Aristotle™ was conducted using blood samples from 788 subjects across 10 cancer types and 2,064 subjects without cancer, with planning for the final clinical validation of Aristotle™ currently underway.

Results from the early validation studies have demonstrated Aristotle™'s high sensitivity and specificity for each cancer, as seen in Figure 23. The Figure displays the **AUROC (area under the ROC curve)** at optimum threshold levels. The AUROC is a performance measure, with higher numbers reflecting a better model at distinguishing between patients with disease and no disease (e.g., a 0.9 AUC means there is a 90% chance that model will be able to distinguish between positive class and negative class). As sensitivity and specificity are inversely proportional to each other, researchers try to determine the optimum threshold (or levels for each variable) that would yield the better performance, or higher AUROC curve.

Figure 23

ARISTOTLE™ OPTIMUM ROC THRESHOLD



Source: StageZero Life Sciences, Ltd.

Aristotle™'s Clinical Applications

StageZero is using Aristotle™'s capabilities to develop gender-specific cancer detection panels (Figure 24). The Company is developing the first multi-cancer detection panel for women, aimed at detecting nine cancers affecting women: ovarian, bladder, nasopharyngeal, colorectal, stomach, cervical, endometrial, breast, and liver cancer. A multi-cancer detection panel for men, for the diagnosis of prostate, liver, bladder, nasopharyngeal, colorectal, and stomach cancer, is in development.

Figure 24

ARISTOTLE™ GENDER-SPECIFIC PANELS

WOMEN'S PANEL		MEN'S PANEL	
	Ovarian Bladder Nasopharyngeal Colorectal Stomach Cervical		Prostate Liver Bladder Nasopharyngeal Colorectal Stomach
	Endometrail Breast Liver		

Source: StageZero Life Sciences, Ltd.

StageZero also plans to expand Aristotle™'s capabilities for applications beyond cancer. The Company's researchers are working on solutions for diseases in the following areas:

- Neuroscience: Schizophrenia and Parkinson's
- Gastroenterology: Inflammatory Bowel Disease and Crohn's
- Cardiovascular: Heart Failure and Chagas Disease
- Musculoskeletal: Rheumatoid Arthritis and Osteoarthritis

Aristotle™'s Market Potential

According to StageZero, Aristotle™, as potentially the first multiple, discrete cancer diagnostic test from a single sample of blood, could realize a $2 billion revenue opportunity. The Company believes that Aristotle™'s ability to recognize not only the presence of cancer, but to identify the type of cancer with a high degree of sensitivity and specificity—to their knowledge, the first blood cancer detection panel to be able to do so—coupled with Aristotle™'s proven and validated technology, provides a significant advantage over other tests that cannot characterized the type of cancer present.

Commercial Activities

The Company's mission of improving health outcomes relies on its ability to provide physicians and their patients with actionable clinical data for cancer risk assessment and diagnosis. The ultimate goal is for StageZero's early cancer diagnostic tests to be offered as risk stratification during a patient's regular medical visits, or as requested by high risk patients. As a prelude to this, in 2017, StageZero began the process of collecting and sharing aggregated data in an effort to help practices and healthcare systems better understand their patient populations and build effective programs to improve patient compliance with cancer screening. The Company expects the data to be an asset and expanded this initiative by commencing research programs with key high-risk groups.

The global market for diagnostic biomarkers is expected to reach roughly $30.6 billion in 2020, growing at a compound annual growth rate (CAGR) of 16% from 2013 to 2020 (Source: Biomarkers Market [Diagnostic Applications in Risk Assessment, Molecular Diagnostics, Disease Diagnosis, Drug Discovery & Development, Drug Formulation, Forensic Applications and Others] – Global Industry Analysis, Emerging Technologies, Competitive Intelligence, Growth Trends, Size, Share, Opportunities and Forecast, 2013–2020, December 10, 2013). This market is being driven by several influences, including further adoption of pharmacogenomics and personalized medicine, high disposable income, increased availability of various tests, and an increase in chronic diseases stemming from an aging population.

Roughly 80% of treatment decisions are based on results from in vitro diagnostic tests, yet diagnostic companies account for less than 2% of total healthcare expenditure (Source: Kalorama, Datamonitor and Visiongain reports). Molecular diagnostic tests based on genomic technologies, such as StageZero's core Sentinel Principle® technology and its ColonSentry® test, are rapidly gaining prominence and acceptance due to their ability to detect and stage disease, monitor treatment, and predict prognosis in a less invasive manner and with superior clinical performance when compared to certain traditional methods.

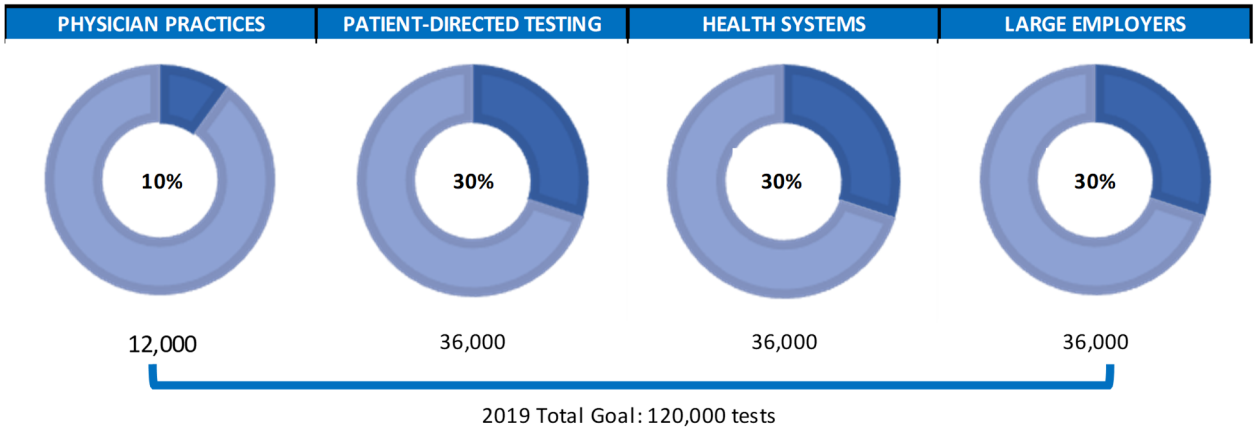
The accompanying section profiles StageZero's technologies and those which may compete with its products, as well as its Aristotle™ screen, which is in development within the liquid biopsy arena.

The typical path to commercialization of new, novel diagnostics is often lengthy and involves many steps, with limited uptake and adoption due to, among other things, medical billing companies' long initiation cycle and uncertainty of their acceptance, reimbursement amount, and payment timeframe for new tests. The Company is relying on its extensive data library to develop a commercialization plan that aims to shorten this cycle, thereby driving adoption and increasing utilization of its tests. Supported by its company-wide efforts and strategic alliances, StageZero has targeted four key medical market segments that would accelerate and advance the uptake and adoption of the Company's proprietary cancer tests, as seen in Figure 25:

- Small clinical and physician practices;
- Telemedicine–consumer-directed;
- Large healthcare systems; and
- Large employers/high risk populations.

Figure 25

MARKET SEGMENTATION



Source: StageZero Life Sciences, Ltd.

The Company believes that the combination of four different markets provides benefits in terms of both adoption rates and revenue. By targeting small physician practices and direct-to-consumer telemedicine options, the Company aims to quickly accelerate the short- and mid-term adoption and revenue generation of its products. In addition, by targeting large healthcare systems and networks, as well as high-risk groups/employers, StageZero believes it is establishing a strong base for the widespread adoption of its products and services within hospitals, clinical integrated networks, physician groups, and other healthcare organizations.

A key strategic component of its commercialization plan is the form of payment for the Company's products related to each market segment. In order to circumnavigate the long and complicated billing process normally associated with medical billing and insurance companies, StageZero is seeking to rely on flat-fee and direct-to-client billing. In terms of direct-to-consumer telehealth efforts, the Company bills the consumer or network a predetermined fee for each of its tests. In addition, by contracting with large healthcare systems and employees, the Company receives an established payment amount for each processed sample. This model can be adopted if the healthcare system provides services through integrated provider networks, self-funded employee plans, or value-based reimbursement systems. Payment to the Company is therefore reliable and predictable. The reimbursement strategy for each segment is as follows:

- Small clinical and physician practices: standard billing to insurers/CMS
- Telemedicine–direct to consumer: cash price or invoiced to networks with payment within 45 days
- Large healthcare systems: fixed price per test, invoiced, and paid within 45 days
- Large employers/high risk populations: cash price collected immediately

StageZero anticipates small practices to account for 10% of its product volume, with direct testing (Telehealth), large healthcare systems, and high-risk population/self-funded employer plans contributing the remaining 90% of its screening test volume. In order to support the sale of its products throughout these channels, the Company has strengthened its sales force through internal channels as well as the execution of two key strategic partnerships: Coastal Medical and Oncore Pharma.

Coastal Medical

On July 2019, StageZero announced the expansion of its U.S. salesforce though its partnership with Coastal Medical, a privately held regional sales organization specializing in selling advanced diagnostic testing solutions to physician practices and hospital systems throughout southeastern U.S. Initial efforts will concentrate on increasing the outreach of the Company's products by selling StageZero's tests in Georgia and South Carolina, before expanding to other states.

Oncore Pharma

On June 2019, StageZero executed a Global Distribution Contract with Oncore Pharma, which aims to commercialize ColonSentry® in all countries other than the U.S., under an exclusive license. The 5-year licensing agreement will initially focus on the Netherlands, Belgium, Luxemburg, Germany, France, Switzerland, Austria, Spain, Monaco, Italy, Portugal, United Kingdom, Ireland, Norway, Sweden, Finland, Denmark, Israel, and the United Arab Emirates, as well as Canada (where Oncore Pharma will work together with the Company).

The partnership aims to deploy a total of 1,750,000 ColonSentry® tests over the next 5 years. Under the terms of the agreement, StageZero will receive a fixed fee per ColonSentry® test, a special royalty payment equal to 10% of Oncore's yearly profits, and one million shares of Oncore Pharma. The processing of ColonSentry® will be done in the Company's Richmond, Virginia laboratory.

On October 2019, Oncore Pharma signed a multi-year agreement with BodyCheck NL for the distribution and sale of ColonSentry® throughout the Netherlands, Belgium, and Luxembourg (Benelux). According to the multi-year agreement, the initial term of six months will be used to implement and launch a sales and marketing campaign. A minimum of 275,000 ColonSentry® diagnostic tests are anticipated to be processed through this relationship. According to Company estimates, the multi-year agreement has a value to StageZero of $40 million. Oncore believes this agreement to be the initial entry point into the European market and plans to expand its geographic reach both in Europe and beyond during 2020.

PHYSICIAN PRACTICES

Small independent physician practices, ranging in size from 1 to 10 providers, are an important sector of the market. The Company is steadily expanding its physician's network and has significantly restructured and upgraded its billing procedures, with reimbursement for the tests coming via billing to insurers and patient-pay. The Company expects this segment to contribute about 10% of its test volume. StageZero believes that its products lend physicians the tools to provide their patients with enhanced services and better overall care. StageZero's easy-to-read reports identify a patients' cancer risks and provide guidance for appropriate clinical interventions, which could help address patients who are non-compliant with annual cancer screening.

Figure 26
MyCancerRisk MATERIALS

Source: StageZero Life Sciences, Ltd.

StageZero's services could also help concierge physicians build and enhance their executive health/wellness programs. The Company has strengthened its efforts to market to concierge physicians whose practice models are more likely to attract patients who want to be proactive about their health and are willing to participate in advanced biomarker testing for early cancer detection. These patients have more disposable income and are more likely to pay out-of-pocket for these tests. As such, the growth of the Company's physician practice network helps it achieve the partnerships and infrastructure required to support a patient-directed testing model in the form of its telehealth program. To support this effort, the Company offers physicians with white label materials from its MyCancerRisk™ program (detailed on page 40) for their practice, including MyCancerRisk™ patient trifolds (Figure 26), posters, patient letters, text for their website, and radio/video spots for use in their practice lobby/hold music.

TELEHEALTH—PATIENT-DIRECTED TESTING

The use of digital technologies to deliver medical care and public healthcare services by connecting multiple users from distinct locations is known as telehealth. This includes technology-enabled healthcare services, telemedicine, and services such as monitoring, assessment, communications, education, and prevention. Technology and telecommunications are used in telehealth to deliver healthcare services outside of traditional healthcare facilities. Patients that want to control their medical care decisions are driving the growth of telehealth services, with the global telehealth market anticipated to reach $16.7 billion by 2025 (Source: Market Study Report, LLC's *Telehealth Market: Market Size & Forecast, 2017 – 2025*, March 2019). In a recent U.S. survey, 66% of people were willing to use telehealth services (Source: American Well®'s *Telehealth Index: 2019 Consumer Survey*). Companies that use telehealth to facilitate direct-to-consumer testing should be rewarded with loyal patients who want personalized care on their terms.

StageZero has been building out its capability in telehealth by assembling partnerships and building the infrastructure required to support a patient-directed testing model. The Company's model requires a system by which patients can request the tests, pay for them, and receive the results; a national network of physicians to review and authorize the tests as well as contact those with elevated results; national capability to draw the blood via mobile as well as "brick and mortar" blood draw sites; and a marketing campaign to raise awareness of its products. To this end, StageZero has partnered with national virtual care companies and provider networks to enable access to over 200 physician networks who will facilitate and authorize diagnostic testing and provide guidance with test results and built a national blood draw network that includes a combination of more than 8,000 draw sites and mobile phlebotomists through various partnerships with clinical laboratories.

MyCancerRisk™

A key initiative to support the Company's telehealth efforts is the development of MyCancerRisk™ (Figure 27), a website portal and data analytic platform. MyCancerRisk.com is an online portal where patients can get information about the Company's products and/or purchase and initiate testing. The portal allows patients to pay one flat fee for the test, the physician order and consult, and phlebotomy (blood draw) services. Once an order is submitted, StageZero connects the patient with a physician within its network who can prescribe the test and discuss the results with patients. Patients are advised to share test reports with their regular healthcare providers so their results can be integrated into their existing medical records as well as current or future treatment plans. If a patient wants to conduct the process through their regular physician, they can alternatively download the patient/physician discussion guide to take to their next doctor's appointment.

Figure 27

MyCancerRisk.com

Source: StageZero Life Sciences, Ltd.

On March 2019, StageZero launched the first of several initiatives to make patient-directed testing available nationwide. The Company partnered with PWNHealth, a national virtual care company that enables access to physicians who facilitate and authorize diagnostic testing and provide guidance with test results. The first test available for online purchase is the Prostate Health Index (*phi*), an FDA approved test that can help physicians differentiate prostate cancer from benign prostatic conditions in men with elevated PSA. The Company has begun to process initial patient orders for the *phi* test.

Patients can initiate a request for the *phi* test online at www.mycancerrisk.com. Once an order is submitted, StageZero connects the patient with a physician in its U.S.-based telehealth partner network who can prescribe the test after confirming the patient is eligible. The Company then connects the patient with a convenient blood draw location or mobile phlebotomist. The test is processed at StageZero's CLIA- and CAP-accredited reference laboratory located in Richmond, Virginia. Results are reported back to the ordering telehealth physician who reviews the results with the patient. Patients pay a flat fee of $299, which covers the physician order, blood draw charges, the test, and physician consult as required.

The Company is supporting the growth of its telehealth initiative with the launch of a national marketing campaign that includes social media marketing, digital advertising, and print media. In addition, the Company expects to add new partners that can help accelerate exposure and uptake of all four tests. StageZero's telehealth initiative, anticipated to be 30% of the Company's test volume in 2019, highlights key aspects of its business strategy. Telehealth is an immediate cash paying model and meets the needs of patients who want greater access to these types of tests.

Prostate Program

To support its telehealth *phi* initiative, the Company launched an awareness campaign for prostate cancer. The campaign uses Gary the Prostate (Figure 28) to explore prostate cancer symptoms, tests, and treatments options. The program includes information on the website, as well as videos on different social media platforms, and advocates for "at risk" men to speak with their physicians about getting tested.

Figure 28

GARY THE PROSTATE

Source: StageZero Life Sciences, Ltd.

The Company also used Gary the Prostate to launch a new online marketing initiative for prostate cancer awareness month. The campaign, which was part of its ongoing patient-directed testing initiative, deployed both paid and organic search and social media campaigns to create awareness for *phi*. In just the four-week September 2019 period, the Company piqued the interest of over 150,000 people searching for more information on prostate cancer. In that time, more than 6,700 prospective patients clicked through to MyCancerRisk.com landing pages (2.6% Facebook and 8.5% Google Ads versus the industry average of 2.5%). The Company is currently processing those patients that provided contact information and asked for information about having the test done.

HEALTH PLANS AND HEALTH SYSTEMS

Moving forward, a large part of the Company's commercial strategy is expected to focus on larger opportunities that can create high volumes of tests as well as generate direct revenue from immediate payment or flat fee invoicing. To support this strategy, the Company plans to conduct strategic alliances to accelerate the adoption of StageZero's menu of proprietary cancer tests with large multi-entity healthcare systems, hospitals, clinical integrated networks, physician groups, and other healthcare organizations. Examples of these strategic alliances include partnerships with JTS Health Partners and LifeX™.

JTS Health Partners

The Company's collaboration with JTS Health Partners (www.jtshealthpartners.com), announced in March 2016, strengthened StageZero's commercialization path by accelerating the adoption of its menu of proprietary cancer tests with large healthcare organizations. JTS is a healthcare management consulting and professional services firm specializing in assisting top healthcare organizations in both the private and public sector in the areas of healthcare information management, data analytics, financial and revenue cycle management, as well as operational performance improvement initiatives for hospitals and physicians.

Under the Agreement, JTS will work to pursue and secure multi-year agreements with hospitals, clinical integrated networks, physician groups, and healthcare organizations for the Company's risk assessment testing services. As part of the partnership, JTS will provide StageZero with management consulting services, assisting with the implementation of billing practices to help the Company maximize revenue collection. The Agreement has an initial term of five years and is renewable annually thereafter by mutual consent

LifeX Ventures

On August 2018, the Company announced a partnership with Pittsburgh-based, LifeX™, a strategic engine for developing cutting-edge, life-saving healthcare solutions and bringing these innovations to market. StageZero plans to work with LifeX™ to develop strategies for incorporating several proprietary, early cancer diagnostics into healthcare settings to improve patient compliance with cancer screening, as well as to bridge the diagnostic gaps in current screening procedures.

The Company plans to combine its unique patient-oriented experiences and capabilities with those of its two partners in the large healthcare organizations marketplace—JTS and LifeX™—to develop and implement value and quality-based reimbursement models that drive enterprise cost reduction for healthcare systems and large employers through the early cancer intervention products of StageZero. These partnerships support the Company's business development initiatives to target larger healthcare systems that can work with high-risk populations and follow-up with patients who have elevated test scores. The Company has experienced early success with a Midwest hospital system that is utilizing all four blood-based cancer biomarker tests in three high-risk patient populations.

StageZero considers large healthcare systems, a network of multiple hospitals and several thousand physicians normally owned by a healthcare plan, as one of its largest business opportunities. This stems from two facts: the large number of patients each system can provide, and a flat fee per test, invoiced and paid within 45 days. However, implementation of the Company programs on these massive organizations is complex, with a sales cycle of over two years. StageZero is relying on its company-wide efforts, as well as strategic alliances, to secure multi-year agreements with hospitals, clinically integrated networks, large physician groups, and healthcare organizations to administer the Company's risk assessment tests. As a result of these efforts, StageZero is currently in implementation discussions with several groups. An example is its recent alliance with Mercer.

The Company has experienced early success with a Midwest hospital system and has initiated a contract with a large healthcare system to offer its array of cancer screening tools. StageZero believes that the basis for large healthcare systems' adoption of its products and services relies on two key benefits that the Company can provide: increased revenue and cost savings. In terms of revenue, StageZero's tests have been proven to address the current cancer screening gap, bringing non-compliant populations to the healthcare environment for the required tests. In addition, by stratifying the population by cancer risks, the Company's products can detect cancer earlier or rule out unnecessary expensive follow-up tests, which can lead to cost savings for both the patient and the healthcare system.

Figure 29

LARGE HEALTHCARE SYSTEM - OPPORTUNITY OVERVIEW

$19 Billion Revenue System	2400 Medical Practitioners
1,200 Clinics	$30 Million Opportunity
Goals	
Get non-compliant patients screened	Reduce costs to Health Insurance Plan
Increase revenue to healthcare system	Collect data to practice intelligent medicine

Source: StageZero Life Sciences, Ltd.

LARGE EMPLOYERS

Early detection of cancer as well as risk stratification is of critical importance in workers exposed to carcinogens. As part of its strategy to focus on larger opportunities that can create high volumes of tests, StageZero is targeting self-funded and large employer healthcare plans with companies that operate in high-risk environments with a higher prevalence of cancer. The type of employers targeted by the Company include firefighters, oil and gas, coal and chemical plants, pilots and flight attendants, drivers, the military, as well as individual States who have specific populations that need screening. The Company currently offers large employers its full panel (colorectal, lung, prostate, and breast cancer tests), and invoices a flat fee on a monthly basis. Reimbursement to the Company is direct and either immediate, or within 45 days upon invoice.

Cancer is the main reason for a catastrophic claim for employer healthcare plans. Thus, the Company's ability to detect cancer early, avoiding the high costs associated with late-stage treatments, provides large employers with self-funded healthcare plans with significant benefits. According to StageZero, employers can achieve cost savings of 20% through early cancer identification and intervention. In addition, stratification of employers by cancer risk also can provide improved employee relations. Motivating non-compliant employees to participate in annual cancer screening, and thus addressing gaps in current screening methods, can improve patient outcomes, retention, and reduce absenteeism (Source: *2017 Sun Life Stop-Loss Research Report*).

StageZero is currently working with multiple high-risk employee partners across the country, initiating screening with firefighter groups, and is in discussions with several self-funded employer plans that have significant interest in the Company's programs.

Firefighters

A key high-risk demographic that the Company has been working with is firefighters. Studies conducted by the National Institute for Occupational Safety and Health (NIOSH) focused on firefighter cancer concluded that firefighters face a 9% increase in cancer diagnoses and a 14% increase in cancer-related deaths, compared to the general population (Source: National Fire Protection Association [NFPA]). These studies have shown significantly increased risks in firefighters for the following cancers: colon, rectal, lung, prostate, melanoma, non-melanoma skin cancer, mesothelioma, multiple myeloma, non-Hodgkin's lymphoma, and stomach (Source: NFPA Journal's *Facing Cancer*, 2017).

Cancer is the leading cause of line-of-duty death among firefighters in the U.S., accounting for 61% of career firefighter deaths between 2002 and 2017, with 1,053 deaths during this period. Since 2002, almost two out of every three firefighters who died in the line of duty died of cancer, according to the International Association of Firefighters.

StageZero has run thousands of tests on firefighters using its advanced biomarker tests for colorectal, lung, prostate, and breast cancers. According to the Company, tests on two fire districts in 2018 reported cancer risks among firefighters far greater than the general population, with 41% and 34% of firefighters evaluated reporting elevated scores in each district, respectively. By detecting cancer earlier, by sending those with high scores to advance screenings, and by reevaluating those with average scores on a yearly basis, Stage Zero believes it can help protect firefighters from the dangers of cancer.

Large Employer Opportunity

The Company has been engaged with another large employer for the use of its products. The target company has over 100,000 employees, a number of which work in high risk areas. StageZero aims to show its ability to reduce catastrophic claims, delivering cost savings to the employer, and at the same time providing enhanced healthcare benefits to employees by giving them the necessary tools for early cancer detection. StageZero plans to start its program in one state and move to a national level during 2020. According to the Company, if it reaches 30,000 of those employees with three test each, it could achieve revenues of $30 million in a given year.

Investment Highlights

- StageZero Life Sciences, Ltd ("StageZero" or "the Company") is a revenue-generating innovator in the liquid biopsy space, focused on developing and commercializing proprietary blood-based diagnostic solutions to aid in the detection of cancer at the earliest possible stage, as well as other disease states.
- The Company's proprietary Sentinel Principle® technology platform is a liquid biopsy technology that uses a blood sample to detect cancer and other disease. The technology is based on the scientific observation that circulating blood reflects, in a detectable way, what is occurring throughout the body. Thus, by conducting a minimally invasive blood draw, the Company can analyze the blood sample to detect cancer and other diseases.
- StageZero believes that its products can improve a patient's prognosis. Early detection of cancer has been proven to improve survival rates and quality of life, and yet 40% of screenable cancers are diagnosed late.
- The science behind the Sentinel Principle® led to the development of the Company's flagship product, ColonSentry®, a blood-based test for assessing an individual's risk of having colorectal cancer (CRC). Initially developed from a clinical study involving approximately 10,000 subjects, ColonSentry® was commercialized in 2014 and has been used successfully in over 100,000 patients throughout the U.S.
    - ColonSentry® is a patient-friendly, blood-based test that can be easily incorporated into a patient's routine annual exam, providing significant clinical advantages: (1) patients are two-times more likely to comply with a colonoscopy following an elevated ColonSentry® score; (2) it increases the effectiveness of colonoscopies, detecting 2.1 to 4.7 times more CRC lesions following a ColonSentry® test; and (3) it provides financial benefits reducing healthcare costs by more than 20% through early interventions.
- StageZero also offers diagnostics tests to assess the probability of having four of the most prevalent cancers: CRC, lung (*Early*CDT®-Lung), prostate (Prostate Health Index [*phi*]), and breast cancer (BreastSentry™).
- StageZero is utilizing its Sentinel Principle® technology for the development of its next generation test, Aristotle™, expected to launch in 2021. Aristotle™ is a multi-cancer panel for the simultaneous screening of 10 cancers (CRC, prostate, cervical, endometrial, breast, ovarian, liver, bladder, nasopharyngeal, and stomach cancer) from a single blood sample.
    - The Company is also planning to expand the applications of Aristotle™ beyond oncology, to help in the diagnosis of disease in gastroenterology, neurology, cardiology, and autoimmune disorders.
- The Company's commercialization strategy aims to shorten the lengthy market-entry process of new diagnostic tests, targeting four market segments: (1) physician practices; (2) telemedicine–consumer directed; (3) large healthcare systems; and (4) large employers/high risk populations.
    - On March 2019, StageZero launched its first nationwide telehealth initiative, making its *phi* test available for online purchase through its portal mycancerrisk.com. The Company has begun to process initial patient orders.
    - The Company has experienced early success with a Midwest hospital system. It has initiated a contract with a large healthcare system to offer its array of cancer screening tools and has engaged with other healthcare groups.
    - In the large employer/high risk market, StageZero began screening firefighter groups, and has been engaged with another large employer, with over 100,000 employees, for the use of its products.
- The Company also operates a CAP-accredited and CLIA-certified laboratory based in Richmond, Virginia that conducts sample processing for the ColonSentry® test as well as for the licensed biomarker tests for lung, breast, and prostate cancers.
- StageZero's long term goals center around two key milestones: achieving profitability (2020) and launching the Aristotle™ test (2021). As of September 30, 2019, the Company had $411,445 in cash and cash equivalents.

Competition

StageZero operates within the biotechnology, molecular diagnostic, and genomic biomarker industry—an industry that is characterized by extensive research and development efforts, rapid technological changes, and strong competition. The Company's competitors include large diagnostic, biotechnology, and other companies; universities; and research institutions. Some of these competitors develop, manufacture, market, and commercialize products and technologies that may compete with StageZero. The basis for the Company's technology is to fill a need for better risk assessment at the primary care physician level, ensuring that high risk patients receive early follow-up testing. StageZero is restructuring, with the formation of IDL, positioning it to take advantage of the projected growth in the molecular diagnostics market. StageZero's successful launch of its ColonSentry® product provides a solid commercial footing, while new tests are being added to the Company's menu of services.

StageZero may compete with companies and institutions offering both molecular and conventional diagnostic products, as well as with companies focused on a single disease area or those developing other technology platform-based tests. Competitive factors that can influence the success of a diagnostic test include clinical performance parameters, such as sensitivity and specificity, invasiveness, acceptance by the medical community, price, reimbursement from state-sponsored health insurance programs (including Medicare and other third-party payers), distribution channels, and patent protection.

ColonSentry® Competition

ColonSentry® is targeting higher risk patients who are over 50 years old and have refused colonoscopy or are unwilling to undergo current colorectal cancer (CRC) screening options. The ColonSentry® test is easily incorporated into an individual's annual exam by primary care physicians, requiring only a simple blood draw, which is delivered to IDL for processing. Unlike stool tests, ColonSentry® is not a 'yes or no test' but provides an actual risk score for a patient.

There are a variety of CRC screening and diagnostic methods in use today, including colonoscopy, flexible sigmoidoscopy, guaiac-based fecal occult blood testing (G-FOBT), immunochemical FOBT, and virtual colonoscopy. Poor patient compliance limits these established methods. According to an American Cancer Society survey of 2010 data (Colorectal Cancer Facts & Figures 2014-2016), only 8.8% of Americans over the age of 50 comply with stool samples for CRC testing and less than 10% of stool collection kits given to patients are ever returned with a stool sample for testing. For the same group, an average of only 56.4% get a CRC endoscopy (average compliance is lower in minority groups). Due to these limitations, a number of companies have developed new stool- and blood-based tests for CRC detection.

Importantly, alternative tests, such as computed tomography (CT), colonography (virtual colonoscopy), or Cologuard, do not count towards population health measurements of CRC screening rates. Furthermore, if these tests are performed and a positive result is found, the patient is no longer preventative screening but now is diagnostic when referred for colonoscopy (meaning that the patient has a 20% financial responsibility for the colonoscopy, facility, anesthesia, pathology, etc.) This compares to StageZero's ColonSentry®, which is a risk stratification test that leads to USPSTF-recommended test (FIT or colonoscopy) and preserves the patient as being seen for a preventive screening service, without financial responsibility, when referred for colonoscopy.

A selection of primary competitors to StageZero's ColonSentry®—either with marketed products or ones in development—are described below.

- Exact Sciences Corp. of Madison, WI (EXAS-NASDAQ) received FDA approval in 2014 to begin selling its Cologuard test in the U.S. markets. Cologuard is a stool-based test that combines a standard Fecal Immunochemistry Test (FIT) and a series of molecular tests.

- Epigenomics AG of Berlin, Germany (EPGNY-OTC) received FDA approval in 2016 for its EpiproColon® test, which is a blood-based test that uses a single DNA biomarker (called Septin9) to detect the presence of CRC.

- VolitionRx Limited (VNRX-NYSE), with headquarters in Singapore, is developing its Nu.Q Colorectal Cancer Screening Triage Test. This test works in conjunction with the current standard screening test (the fecal immunochemical test [FIT]) to measure nucleosomes in the blood stream.

***Early*CDT®-Lung Test Competition**

Competitors to StageZero's *Early*CDT®-Lung test are described below.

- Epigenomics AG of Berlin, Germany (EPGNY-OTC) is currently marketing Epi proLung BL Reflex Assay in Europe as a CE-marked in vitro diagnostic device (IVD), which is under review by the U.S. FDA. Increased DNA methylation of the SHOX2 gene, as measured by this assay, purports to indicate the presence of lung cancer.

- Genesys Biolabs of Rockville, MD (a business unit of 20/20 Genesystems, Inc.), is currently marketing PAULA's Test (Protein Assay Using Lung cancer Analytes), where a blood sample is used to analyze a panel of four protein markers (three tumor antigens and one tumor autoantibody) associated with lung cancer.

- Biodesix, Inc. of Boulder, CO is marketing BDX-XL2 to measure the relative abundance of two plasma proteins, LG3BP and C163A, in patients with a pretest probability of cancer (pCA) ≤ 50%.

- OncoCyte Corp. of Alameda, CA (OCX-NYSE) is currently developing DetermaVu™ as a confirmatory test for presence or absence of lung cancer to reduce the need for unnecessary invasive biopsies when suspicious lung nodules are detected by imaging modalities, such as x-rays or other scans.

- LungLife AI Inc. of Thousand Oaks, CA is a cancer diagnostics company focused on transforming cancer diagnosis and management through the artificial intelligence (AI) enabled molecular analysis of cancer biomarkers in blood. The company is focused on lung cancer diagnostic solutions, with its testing methodology designed to deliver actionable information to clinicians via a minimally invasive blood draw. Its tests span all stages of lung cancer, from an aid in diagnosis for patients with suspicious lung nodules as well as treatment stratification and monitoring in late-stage lung cancer.

Prostate Health Index (*phi*) Competition

Competitors to StageZero's Prostate Health Index (*phi*) are described below.

- Hologic, Inc. (HOLX-NASDAQ) of Marlborough, MA, has developed the Progensa®PCA3 assay, which is FDA approved as the first urine-based molecular test to measures the concentration of prostate cancer gene 3 (PCA3) and PSA RNA molecules in postdigital rectal (DRE) male urine specimens.

- Belgium-based MDxHealth (MDXH-EBR) is currently marketing SelectMDx and ConfirmMDx for prostate cancer. SelectMDx helps identify patients at increased risk for aggressive disease, thereby aiding in the selection of men for prostate biopsy. ConfirmMDx is intended for men with a previous negative prostate biopsy to assist urologists in identifying truly negative men who may forego an unnecessary repeat biopsy procedure.

- OPKO Health of Miami, FL (OPK-NASDAQ) is marketing 4Kscore Test, which combines four prostate-specific kallikrein assay results with clinical information in an algorithm to calculate the individual's percent risk for aggressive prostate cancer.

- Exosome Diagnostics of Waltham, MA is marketing ExoDx®Prostate (IntelliScore), which is a urine-based test for use with PSA and other factors (age, race, and family history) to enable physicians to predict whether a patient presenting for an initial biopsy does not have high-grade prostate cancer.

BreastSentry™ Competition

Competitors to StageZero's BreastSentry™ are described below.

- Genomic Health of Redwood City, CA (GHDX-NASDAQ) has developed Oncotype Dx®, a test that can predict the likelihood of chemotherapy benefit as well as the chance of cancer recurrence in patients with early stage breast cancer. Oncotype Dx® is intended for use in all newly diagnosed patients with early-stage breast cancer who have node-negative or node-positive, estrogen receptor-positive, HER2-negative disease.

- Agendia N.V. of Amsterdam, Netherlands has developed Mammaprint®, an FDA approved test to assess the risk that a breast tumor will metastasize to other parts of the body in order to determine whether or not each patient will benefit from chemotherapy.

- Janssen Diagnostics (a Johnson and Johnson [JNJ-NYSE] company) has developed the CELLSEARCH® Circulating Tumor Cell blood test to assess the prognosis of patients with metastatic cancer and monitor therapeutic response. This test is FDA cleared and is performed by Quest Diagnostics.

Aristotle™ Competition (In Development) for Cancer Liquid Biopsies

Population-based cancer screening is currently a hit-and-miss process. Computed tomography, colonoscopy, Pap testing, and mammography have demonstrated varying degrees of benefit for reducing deaths from lung cancer, colorectal cancer, cervical cancer, and breast cancer, respectively, but the continued mortality from those conditions underlines the shortcomings of these methods. For many other types of cancer, including pancreatic and liver cancer, there are no effective screening tests. For liquid biopsy technology, there is ample opportunity in which to bring a novel approach to cancer screening, however, developing an understanding of the clinical significance of a test result is equally as important as developing an accurate test. Companies such as StageZero, which operate within this space continue to develop their products, seeking to answer the following crucial questions: (1) which biological signals to look for, (2) how to interpret the results, and (3) which indications to focus on. Within this space, competitors are seeking to differentiate themselves across these key parameters.

The idea behind liquid biopsy tests is to accompany confirmed cancer diagnoses by gathering meaningful insights from small amounts of circulating tumor DNA (ctDNA). StageZero is creating technology to give access to patient friendly, blood-based tests that can detect disease at its earliest stages. StageZero believes that its technology could become highly disruptive to the diagnostic industry, especially in situations when multiple disease states can be screened from a single sample of blood. Allowing early diagnosis to commence at the population level has implications for many areas, including self-funded employer plans with employees in high-risk environments, including firefighters, employees working in oil and gas, coal and chemical plants, pilots and flight attendants, drivers; large healthcare systems, especially those with outreach programs and benefit plans; the military; as well as individual states who have specific populations which need screening.

StageZero's Aristotle™ is being developed as the first multiple, discrete cancer diagnostic test from a single sample of blood. The test is seeking to expand the Company's offering into this commercial framework. StageZero believes there is a $35 billion opportunity in the early diagnosis of cancer via an affordable, patient-friendly test. Aristotle™ is being developed as a test for ten discrete cancers from a single sample of blood, with data thus far indicating high sensitivity and specificity across the individual cancers. The Company expects to have the full clinical validation completed within two years.

There are various potential competitors to Aristotle™, as summarized in Figure 30 and described below.

Figure 30
SELECTED LIQUID BIOPSY TESTS FOR CANCER

Company	Products	Technology	Status
Adaptive Biotechnologies	ClonoSEQ	Test employing multiplex polymerase chain reaction (PCR) and next-generation sequencing (NGS) for detecting minimal residual disease in acute lymphoblastic leukemia or multiple myeloma	FDA approval 28 September 2018
Epic Sciences, Genomic Health	Oncotype DX AR-V7 Nucleus Detect	Test that detects AR-V7 protein in the nucleus of circulating tumor cells to guide treatment selection for patients with metastatic castration-resistant prostate cancer	Clinical Laboratory Improvement Amendments (CLIA)-certified test
Epigenomics (Berlin)	Epi proColon	Real-time PCR test for methylated cytosine residues in the *SEPTIN9* gene for detection of colon cancer	FDA approval 13 April 2016
Foundation Medicine	FoundationOne Liquid	Hybrid-capture-based NGS test that detects clinically relevant genomic alterations (substitutions, insertion/deletions, copy number alterations & selected genetic rearrangements) in 70 oncogenes	FDA breakthrough device designation 28 April 2018
Freenome	Freenome multianalyte test for colon cancer	'Multi-omic' test that integrates biological signals from tumors and the immune system for early detection of colorectal cancer	Research stage
GRAIL	Multicancer early detection test	NGS blood test for detecting multiple cancer types by analyzing ctDNA methylation patterns	FDA breakthrough device designation 13 May 2019
Guardant Health	Guardant360; Guardant Omni; Lunar-1; Lunar-2	Commercially available ctDNA test of a 73-gene panel to guide treatment selection in non-small-cell lung carcinoma (NSCLC) (Guardant360); commercially available 500-gene panel for drug development (Guardant Omni); research-use-only test for detecting minimal residual disease and disease recurrence (Lunar-1); development-stage test for early detection of cancer (Lunar-2)	Guardant360, a lab-developed test, received FDA breakthrough device designation 15 February 2018; the other tests are in development
Inivata (Cambridge, UK)	InVisionFirst-Lung	ctDNA blood test employing tagged amplicon sequencing for detecting genomic alterations in a 36-gene panel, including 8 actionable genes relevant to NSCLC	Lab-developed test with Medicare reimbursement
Mirxes (Singapore)	GastroClear	Quantitative PCR (qPCR) assay for a panel of serum microRNA (miRNA) biomarkers of gastric cancer and breast cancer	The Singapore Health Sciences Authority approval 9 May 2019 for gastric cancer; research stage for breast cancer
Oncimmune Holdings (Nottingham, UK)	EarlyCDT-Lung	ELISA that detects seven autoantibodies directed against tumor-associated antigens in plasma	Available worldwide apart from the US; European Union CE Mark 31 May 2018
Resolution Bioscience	Resolution HRD	NGS assay that detects sequence variations in genes associated with homologous recombination deficiency	FDA breakthrough device designation 30 May 2019
Roche Diagnostics	Cobas EGFR Mutation Test v2	Real-time PCR test that detects 42 defined mutations in the epidermal growth factor receptor (EGFR) gene to guide treatment selection in NSCLC	First FDA approval 1 June 2016
Thrive Earlier Detection	CancerSEEK	Multianalyte test that combines multiplexed PCR detection of mutations in ctDNA at 1,933 loci with measurements of validated protein biomarkers to diagnose eight common cancer types	Received FDA breakthrough designation 8 August 2018 for detection of mutations and proteins associated with pancreatic and ovarian cancers

Sources: Company websites, PubMed, Nature Biotechnology 37, 972-974 (2019).

Companies within this space who have commercial offerings, such as Adaptive Biotechnologies and Guardant Health (Redwood City, CA), along with academic investigators, have long spoken of the potential to estimate tumor size, guide treatment selection, monitor resistance to therapy, and detect disease recurrence with liquid biopsy platforms, yet, adoption from clinical practices remains still low. As well, liquid biopsy platform use in population screening presents a complex problem due to the high signal-to-noise ratio within that setting. That said, there is tremendous potential surrounding this technology as demonstrated in the following recently completed financial transactions: Adaptive Biotechnologies (Seattle, WA) completed a $345 million initial public offering (IPO) in July 2019; Freenome (South San Francisco, CA) raised $160 million series B funding also in July 2019; and Thrive Earlier Detection (Cambridge, MA) launched with a $110 million series A round in May 2019. Profiles of the key competitors are provided below.

- Adaptive Biotechnologies Corporation (ADPT-NASDAQ) of Seattle, WA develops an immune medicine platform for the diagnosis and treatment of various diseases. The company offers the immunoSEQ research service and kit, which is used to answer research questions that inform current and future clinical trials, as well as to discover new prognostic and diagnostic signals. It also provides clonoSEQ diagnostic tests, which include immunosequencing services for use in the detection and monitoring of minimal residual disease in patients with select blood cancers. In addition, the company offers a pipeline of clinical products and services that are used for the diagnosing, monitoring, and treating diseases such as cancer, autoimmune conditions, and infectious diseases. Adaptive Biotechnologies has strategic collaborations with Genentech, Inc. to develop, manufacture, and commercialize neoantigen directed T cell therapies to treat a range of cancers; and Microsoft Corporation to develop diagnostic tests for early detection of various diseases from a single blood test. The company was formerly known as Adaptive TCR Corporation and changed its name to Adaptive Biotechnologies Corporation in December 2011. Adaptive Biotechnologies completed a $345 million initial public offering (IPO) in July 2019.

- Biocept, Inc. (BIOC-NASDAQ) of San Diego, CA, is an early stage molecular oncology diagnostics company, developing and commercializing proprietary circulating tumor cell (CTC) and circulating tumor DNA assays utilizing a standard blood sample. The company's cancer assays provide information to healthcare providers to identify oncogenic alterations that qualify a subset of cancer patients for targeted therapy at diagnosis, progression, and monitoring in order to identify resistance mechanisms. The company offers assays for solid tumor indications, such as breast cancer, non-small cell lung cancer, small cell lung cancer, gastric cancer, colorectal cancer, prostate cancer, melanoma, pancreatic biliary cancer, and ovarian cancer, and sells its cancer diagnostic assays directly to oncologists and other physicians at private and group practices, hospitals, and cancer centers in the U.S., as well as markets its clinical trial and research services to pharmaceutical and biopharmaceutical companies, and clinical research organizations.

- Epic Sciences, Inc. of San Diego, CA, is a diagnostics company that develops highly sensitive tests to identify and molecularly characterize circulating tumor cells through a minimally invasive blood sample. The company's platform provides profiles of single cell phenotype and genotype, including phenotypic measures, specific biomarker expression levels, subcellular biomarker localization, morphologic characteristics, genotypic measures, NGS, FISH, single cell genomics capabilities, and CTC detection and characterization capabilities. Epic Sciences also provides Oncotype DX AR-V7 Nucleus Detect test for patients with metastatic castration-resistant prostate cancer; and biopharma solutions. The company partners with biotechnology and pharmaceutical companies and cancer centers around the world.

- Epigenomics AG of Berlin, Germany is a cancer molecular diagnostics company, developing and commercializing blood-based diagnostic tests across multiple cancer indications with high medical needs in Europe, North America, and Asia. Its lead product is Epi proColon, a blood-based test for the early detection of colorectal cancer using its proprietary DNA methylation biomarker, Septin9. The Epi proColon® is based on a real-time polymerase chain reaction (PCR) detection of methylated Septin9 from blood and is the only commercially available blood-based DNA hypermethylation screening test for CRC (32). The test discriminates between patients with CRC and healthy controls with a sensitivity of 75-81% and a specificity of 96-99%. The company also offers Epi proLung, a liquid biopsy test for lung cancer detection; and Epi BiSKit, a pre-analytical tool that provides a set of reagents for the preparation of bisulfite-converted DNA. Epigenomics' development pipeline further contains products for screening, early detection, and diagnosis of colorectal and lung cancers. In addition, Epigenomics engages in

the research and identification of additional DNA methylation biomarkers for prostate, bladder, breast, and ovarian cancers.

- Foundation Medicine, Inc. of Cambridge, MA provides various molecular information products within the U.S. The company's molecular information platform includes proprietary methods and algorithms to analyze specimens across various types of cancer, as well as for incorporating that information into clinical care. As well, the company offers genomic insights about each patient's individual cancer, enabling physicians to optimize treatments in clinical practice and biopharmaceutical companies to develop targeted therapies and immunotherapies. Foundation Medicine provides clinical products, such as FoundationOne for solid tumors; FoundationOne Heme for blood-based cancers, or hematologic malignancies, including leukemia, lymphoma, and sarcomas; Foundation Assay for Circulating Tumor; FoundationFocus CDxBRCA, a diagnostic assay to aid in identifying women with ovarian cancer; and FoundationOne CDx, a diagnostic assay for solid tumors. Foundation Medicine further offers FoundationCORE, a knowledgebase to publish scientific and medical advances, and foster relationships throughout the oncology community. Foundation Medicine has strategic collaboration agreements with F. Hoffmann-La Roche; Genentech; and Novartis. The company also has collaborations with The European Organization for Research and Treatment of Cancer to advance precision medicine using genomic profiling to facilitate clinical trial enrollment; and Merck & Co. to develop companion diagnostic tests for use with KEYTRUDA. It moreover has a three-party collaboration agreement with F. Hoffmann-La Roche and DIAN Diagnostics Group to integrate the company's comprehensive genomic profiling assays into clinical patient care in mainland China; and a collaboration with QED Therapeutics to develop companion diagnostics for infigratinib.

- Freenome Holdings, Inc. of South San Francisco, CA is developing technology for early signs of cancer. Its 'multi-omic' approach looks at cell-free DNA, methylation signatures, and proteins, both from nascent tumors and from the immune system. These signals are then integrated using artificial-intelligence (AI)-driven analytics. The basis for Freenome's approach is that circulating cells of the immune system are detecting and responding to cancer in its earliest stages. Such signals are often ignored as other companies focus their liquid biopsy efforts on the ctDNA fraction shed exclusively by tumors. In one retrospective study, Freenome achieved 85% mean sensitivity (at 85% specificity) for stage I and stage II colorectal cancers testing cell-free DNA from tumor and immune cells, without including any other analytes. Freenome is initially focusing on colorectal cancer, reflecting the fact that colorectal cancer currently has a well-defined screening test—Exact Sciences' Cologuard stool DNA test—against which Freenome can compare its own test. A validation study called AI-Emerge, involving 3,400 participants, including healthy volunteers undergoing routine colonoscopy and people with newly diagnosed colorectal cancer, is underway and is expected to have results early next year.

- GRAIL, Inc. of Menlo Park, CA, which was spun out of NGS technology developer Illumina in 2016 with $900 million in equity raised in 2017 (and raising $1.5 billion in total), has largely abandoned searching for cancer-associated mutations in ctDNA in favor of studying its methylation signatures as an alternative. The company believes that the cell-free DNA methylome provides a richer signal than cancer-associated mutations. Based on a particular region of the genome being investigated, the DNA typically harbors two to three mutations of interest; in contrast, methylation tags are abundant. GRAIL'S sequencing database of cancer and non-cancer methylation signatures covers about 30 million methylation sites across the genome. Beyond indicating the presence—or lack—of cancer, methylation signatures further provide insight into the tissue of origin for any cancer that is detected. This is key in clinical follow-up of patients. The company has stated that it expects to begin a prospective study next year to test its multicancer liquid biopsy diagnostic for multiple cancers, including lung, pancreatic, esophageal, and ovarian.

- Guardant Health, Inc. (GH-NASDAQ) of Redwood City, CA is a precision oncology company that provides blood tests, data sets, and analytics. The company offers liquid biopsy tests for advanced stage cancer, such as Guardant360, a molecular diagnostic test that measures various cancer-related genes; and GuardantOMNI, a broader gene panel, including genes associated with homologous recombination repair deficiency and biomarkers for immuno-oncology applications. It also provides LUNAR-1 for minimal residual disease and recurrence detection in cancer survivors. The company is further developing a liquid biopsy test for early detection of colorectal cancer, called Lunar-2, which combines sequence and epigenomic analyses of ctDNA, as

well as a bioinformatics classification system for eliminating benign clonal mutations arising during hematopoiesis. This study is expected to recruit 10,000 participants with average risk of developing colorectal cancer. Additionally, it offers development services, including companion diagnostic development and regulatory approval, clinical trial referral, and liquid biopsy testing development and support services to biopharmaceutical companies and medical institutions.

- Inivata Limited of Cambridge, UK operates as a clinical cancer genomics company focused on developing applications for circulating tumor DNA (ctDNA) analysis to improve cancer testing and treatment for oncologists and their patients. The company develops TAm-Seq technology that allows the detection and analysis of genomic material from a cancer patient's cell-free ctDNA, which can be collected through blood samples.

- MiRXES Pte. Ltd of Singapore develops life science research tools and molecular diagnostic tests for research and clinical diagnostic use. The company offers RT-qPCR assays, assay panels, spike-in RNA kits, and biomarker discovery solutions.

- Resolution Bioscience Inc. of Kirkland, WA is dedicated to developing a highly sensitive, non-invasive liquid biopsy platform that improves cancer diagnostics and monitoring for patients around the world. The company has developed and patented core technology for circulating cell-free DNA NGS analysis and was the first to demonstrate identification of all four major types of mutations in a blinded, clinical study.

- Roche Diagnostics Corporation of Indianapolis, IN manufactures and sells products and solutions for manufacturers in the diagnostics and pharma biotech industry. It offers diagnostics products for cancer, cardiac health, infectious diseases, and women's health. Roche Diagnostics Corporation operates as a subsidiary of Roche Holding AG. Roche Diagnostic has developed the cobas® EGFR Mutation Test v2, which is a real-time PCR test that identifies 42 mutations in exons 18, 19, 20 and 21 of the epidermal growth factor receptor (EGFR) gene, including the T790M resistance mutation. It is designed to enable testing of both tissue and plasma specimens with a single kit and allows labs to run tissue and plasma on the same plate simultaneously. For optimized workflow results, Roche has developed a cell-free DNA (cfDNA) sample preparation kit to optimize extraction of DNA from plasma.

- Thrive Earlier Detection of Cambridge, MA is tackling multiple indications, seeking to build earlier detection into routine care for 'average-risk individuals.' The company is developing a liquid biopsy platform based on CancerSEEK, a prototype test developed by Nickolas Papadopoulos, Kenneth Kinzler, and Bert Vogelstein of the Sidney Kimmel Comprehensive Cancer Center at Johns Hopkins University. CancerSEEK is a single blood test that provides a unique new framework for early detection of the most common cancers. As a multi-analyte test, CancerSEEK recognizes mutations at 1,933 distinct genetic loci, as well as a panel of validated protein biomarkers of cancer. In a retrospective study of 1,005 patients with confirmed, non-metastatic cancer (stages I-III), CancerSEEK achieved detection rates from 69-98% (>99% specificity) across five cancers (ovary, liver, stomach, pancreas, and esophagus)—all cancers for which there are no screening tests available. A machine-learning-based algorithm localized the tumors to two anatomic sites in a median 83% of patients and to a single organ in a median 63% of patients. CancerSEEK's median sensitivity was 43% for stage I cancers, 73% for stage II cancers, and 78% for stage III cancers. Without any such screening tests for most types of cancer, such sensitivity levels may be sufficiently useful for detecting cancer earlier than what is currently available. CancerSEEK is noninvasive and can, in principle, be administered by primary care providers at the time of other routine blood work. Ideally, cancers could be detected early enough to be cured by surgery alone, but even cancers that are not curable by surgery alone would likely respond better to systemic therapies when there is less advanced disease. It is expected that this test could be used routinely for cancer screening with a cost about the same as or less than other currently available screening tests for single cancers. Thrive is collaborating with Johns Hopkins and the healthcare provider, Geisinger, on a five-year prospective screening study called DETECT, which has enrolled 10,000 healthy female participants ages 65 to 75. An interim data read-out, based on one year of follow-up, is expected in the middle of 2020.

Historical Financial Results

Figures 31, 32, and 33 provide the Company's consolidated statements of loss and comprehensive loss, its consolidated statements of financial position, and its consolidated statements of cash flows for the year ended period ending September 30, 2019.

Figure 31
CONSOLIDATED STATEMENTS OF LOSS AND COMPREHENSIVE LOSS
(EXPRESSED IN U.S. DOLLARS)

	Three-month periods ended September 30		Nine-month periods ended September 30	
	2019	2018	**2019**	2018
	$	$	**$**	$
REVENUES				
	22,968	98,221	**88,729**	115,904
Total Revenues	**22,968**	98,221	**88,729**	115,904
EXPENSES				
Cost of goods sold	**275,750**	300,791	**832,558**	916,848
General and administrative	**1,192,862**	927,182	**3,056,707**	2,552,943
	1,468,612	1,227,973	**3,889,265**	3,469,791
Loss before the undernoted	**(1,445,644)**	(1,129,752)	**(3,800,536)**	(3,353,887)
Gain from reevaluation of warrants	**(3,638,025)**	(548,388)	**(769,507)**	(1,112,913)
Change in fair value of conversion liabilities	**(169,883)**	3,000	**78,240**	616,544
Finance costs	**155,345**	87,622	**1,215,612**	1,022,423
	(3,652,563)	(457,766)	**524,345**	526,054
Total comprehensive income (loss) for the period	**2,206,919**	(671,986)	**(4,324,880)**	(3,879,941)
Basic and diluted income (loss) per common share	**0.01**	(0.01)	**(0.02)**	(0.03)

Source: StageZero Life Sciences Ltd.

Figure 32
CONSOLIDATED STATEMENTS OF FINANCIAL POSITION
(EXPRESSED IN U.S. DOLLARS)

	At September 30, 2019 $	At December 31, 2018 $
ASSETS		
Current		
Cash and cash equivalents	**411,445**	106,228
Trade and other receivables, net	**49,666**	45,102
Inventory	**217,329**	110,958
Short-term portion of prepaid expenses and deposits	**127,212**	90,614
Total current assets	**805,652**	352,902
Non-current assets		
Property, plant and equipment, net	**878,360**	1,068,514
Right of Use Property, net	**843,422**	—
Long-term portion of prepaid expenses and deposits	**25,000**	25,000
Godwill	**1,039,349**	1,039,349
Total non-current assets	**2,786,131**	2,132,863
Total assets	**3,591,783**	2,485,765
LIABILITIES AND SHAREHOLDERS' DEFICIENCY		
Current		
Trade and other payables	**2,311,360**	3,359,875
Short-term portion of warrant liability	**—**	—
Short-term portion of right of use liability	**173,914**	—
Conversion liability	**138,999**	251,000
Short-term portion of notes payable	**1,633,950**	1,904,668
Total current liabilities	**4,258,223**	5,515,543
Non-current liabilities		
Long-term portion of warrant liability	**2,826,593**	419,905
Long-term portion of right of use liability	**684,434**	
Long-term portion of notes payable	**728,396**	1,319,858
Long-term liabilities	**67,340**	67,340
Total non-current liabilities	**4,306,763**	1,807,103
Total liabilities	**8,564,986**	7,322,646
Shareholders' deficiency		
Share capital	**80,550,699**	77,005,842
Contributed surplus	**11,099,012**	10,455,311
Accumulated and other comprehensive income	**1,304,968**	1,304,968
Deficit	**(97,927,882)**	(93,603,002)
Total shareholders' deficiency	**(4,973,203)**	(4,836,881)
Total liabilities and shareholders' deficiency	**3,591,783**	2,485,765

Source: StageZero Life Sciences Ltd.

Figure 33
CONSOLIDATED STATEMENTS OF CASH FLOWS
(EXPRESSED IN U.S. DOLLARS)

	Three-month periods ended September 30		Nine-month periods ended September 30	
	2019	2018	**2019**	2018
	$	$	**$**	$
OPERATING ACTIVITIES				
Net loss for the period	**2,206,919**	(671,986)	**(4,324,880)**	(3,879,941)
Non-cash adjustments				
Finance costs	**155,345**	87,649	**1,215,612**	1,022,450
Share-based compensation	**617,999**	89,314	**643,701**	384,484
Depreciation	**77,956**	71,611	**197,531**	239,758
Change in fair value of conversion liability	**(169,882)**	3,000	**78,240**	616,544
(Gain) on revaluation of warrants	**(3,638,025)**	(548,388)	**(769,507)**	(1,112,913)
	(749,689)	(968,800)	**(2,959,304)**	(2,729,618)
Changes in non-cash working capital balances related to operations				
Trade and other receivables	**33,668**	42,234	**(4,564)**	20,080
Prepaid expenses and deposits	**13,537**	13,689	**(36,598)**	49,412
Inventory	**(2,020)**	(10,041)	**(106,371)**	(55,752)
Trade and other payables	**(2,009,540)**	162,391	**(1,048,515)**	(118,375)
Gain/Loss on Sale of Assets	**—**	—	**27,953**	—
Non-cash change in notes payable	**(122,830)**	(5,632)	**(77,424)**	(3,017)
Cash used in operating activities	**(2,836,874)**	(766,158)	**(4,204,823)**	(2,837,270)
FINANCING ACTIVITIES				
Payment of principal to Health Diagnostic Laboratories Inc.	**(30,000)**	(20,000)	**(90,000)**	(80,000)
Proceeds from issuance of shares and warrants from capital commitment		92,542		805,201
Proceeds from issuance of structured notes payable		—		1,541,800
Proceeds from issuance of convertible notes	**—**	—	**1,027,941**	600,000
Proceeds from issuance of notes payable	**—**	—		234,000
Proceeds from issuance of Units	**2,838,029**	—	**3,972,733**	(18,863)
Payment of note payable and interest	**(314,576)**	—	**(333,007)**	
Lind commitment fee	**—**	—	**(53,795)**	(100,000)
Debt issuance costs	**—**	(6,987)		(117,229)
Share issuance costs	**—**			(52,718)
Cash provided by financing activities	2,493,453	65,555	4,523,872	2,812,191
INVESTING ACTIVITIES				
Leasehold Improvement Lab Equipment in IDL	—	—	**(13,832)**	—
Cash used in investing activities	—	—	**(13,832)**	—
Net increase (decrease) in cash during the period	**(343,421)**	**(700,605)**	**305,217**	(25,079)
Cash, beginning of period	**754,866**	**716,750**	**106,228**	41,224

Source: StageZero Life Sciences Ltd.

Recent Events

April 3, 2020—Announced an abstract entitled "Aristotle: A Single Blood Test for Pan Cancer Screening" was selected for online publication at the annual meeting of the American Society of Clinical Oncology (ASCO). The annual meeting will be a virtual event, rather than the originally planned meeting in Chicago IL, over the time period of May 29-June 2, 2020.

March 31, 2020—Announced that it is preparing to offer testing for COVID-19 in both the U.S. and Canada. StageZero will offer both the serology point-of-care and lab-based PCR tests.

March 31, 2020—Announced it had intended to issue its audited Financial Statements for the calendar year 2019, the Management Discussion and Analysis for the 3 month and 12-month periods to 31 December 2019 and the Annual Information Form on March 30, 2020, in line with its normal reporting calendar. The Company now, however, due to disruption of the audit process caused by the Covid-19 crisis, intends to rely on exemptions recently granted by Canadian securities regulatory authorities that allow it to delay the issue of the 2019 Financial Statements, the 2019 MD&A, and the 2019 AIF.

February 21, 2020—Announced that the Company had closed a private placement Convertible Debenture Financing for gross proceeds of $1,180,000 on February 19, 2020.

January 30, 2020—Announced that the Company is participating in Mercer's new vendor database in the U.S.. The Mercer internal vendor intelligence database is available to Mercer Consultants to be able to do streamlined health and benefits vendor research on behalf of their clients in the U.S.

January 27, 2020—Announced that it closed a private placement financing of $674,408.80.

January 13, 2020—Announced that it retained Fig House Communications to manage all aspects of the Company's investor relations program.

January 3, 2020—Announced conversion of December 2016 Convertible Debentures that matured on December 23, 2019. Canadian $621,000 of outstanding Debentures were converted.

December 9, 2019—Announced that BreastSentry™ and Prostate Health Index tests were added to the licensing and services agreement with Oncore Pharma.

November 15, 2019—Announced Q3 2019 progress update, including operational results for the three-month period ended September 30, 2019 and provided a progress update on its business.

November 14, 2019—Announced that it expanded the Company's telehealth presence with the addition of new partners, including an e-Commerce platform and expansion of in-home mobile phlebotomy.

November 13, 2019—Announced that it will host an investor call for third quarter 2019 results on November 15, 2019.

November 6, 2019—Announced that the ColonSentry® Blood test is now available to consumers through Online Telehealth Platform.

October 10, 2019—Announced that its licensing partner, Oncore Pharma, has signed a multi-year agreement with BodyCheck NL for the distribution and sale of ColonSentry® throughout the Netherlands, Belgium, and Luxembourg (Benelux).

October 2, 2019—Announced that the Company is gaining traction in patient-directed testing following the launch of a new online marketing initiative for prostate cancer awareness month.

September 12, 2019—Announced that the Company would be presenting at this year's Fall Investor Summit on September 16th-17th in New York City.

August 14, 2019—Announced operational results for the three-month period ended June 30, 2019 and provided a progress update on its business.

August 12, 2019—Announced that it will release its second quarter 2019 operational results before markets open on August 14, 2019.

August 7, 2019—Announced that James Howard-Tripp will be presenting at the ii6 Summit, August 8 at the Omni King Edward Hotel in Toronto. The event, which is sponsored by InvestorIntel, gives CEOs an opportunity to present their companies to multiple self-directed, accredited investors.

July 26, 2019—Announced the second closing for $1,043,049 to complete the $3.708 million private placement financing round as approved by shareholders at the Company's Annual and Special Meeting. The private placement is fully subscribed.

July 11, 2019—Announced the first closing for $2,665,418 of the $3.708 million private placement financing round as approved by shareholders at the Company's Annual and Special Meeting. StageZero anticipates a final closing by July 19, 2019. The private placement is fully subscribed.

July 9, 2019—Announced that it is partnering with Coastal Medical, a privately held sales organization in Savannah, GA, to increase outreach to physician practices and hospital systems throughout the Southeast. Coastal Medical is a regional sales organization specializing in selling advanced diagnostic testing solutions throughout the Southeast. Initial efforts will concentrate on selling StageZero testing in Atlanta and South Carolina and expand to other states.

June 26, 2019—StageZero Life Sciences Ltd (formerly GeneNews) announced that beginning June 26, 2019, the Company will be trading under the ticker symbol (TSX: SZLS). Trading will continue in the Company's common shares under the new name, symbol, and CUSIP number. The Company officially changed its name from GeneNews Ltd. to StageZero Life Sciences Ltd on June 20, 2019.

June 20, 2019—Reported that its shareholders voted in favor of all items of business, including the election of all nominee directors listed in the Company's management information circular dated May 15, 2019 at its annual and special meeting of shareholders held on June 19, 2019.

June 17, 2019—Announced that it will host a live webcast that includes an online presentation following the Company's Annual General Meeting of shareholders on Wednesday, June 19, 2019.

June 10, 2019—Announced that it has signed a Global Licensing and Services Agreement with Oncore Pharma, Inc.

May 16, 2019—Announced operational and financial results for the three-month period ended March 31, 2019 and provided a progress update on its business.

May 14, 2019—Announced that Gary the Prostate, the Company's national spokesperson for prostate cancer awareness, has been recently diagnosed with an elevated PSA.

May 9, 2019—Announced that it has launched the Company's first awareness campaign on prostate cancer. The campaign uses Gary the Prostate to explore prostate cancer symptoms, tests, and treatments.

April 22, 2019—Announced that Lind Asset Management XI, LLC has increased its funding under the First Convertible Security of the Convertible Security Funding Agreement dated May 31, 2018 between the Company and Lind by CDN$750,000.

April 17, 2019—Announced the Company has launched its first telehealth program for marketing the Prostate Health Index (*phi*) directly to patients nationwide.

April 3, 2019—Announced operational and financial results for the three-month and twelve-month periods ended December 31, 2018 and provided a progress update on its business.

April 2, 2019—Announced that the CDN $510,000 second tranche of the private placement financing has closed. A total of 14 investors participated in the private placement for total gross proceeds of CDN $510,000.

March 29, 2019—Announced that it will release its fourth quarter 2018 results before markets open on Tuesday, April 2, 2019.

March 28, 2019—Announced that the Company has launched the first of several initiatives to make patient-directed testing available nationwide.

March 25, 2019—Announced the closing of a $1.0 million strategic private placement financing round and, due to high demand, launched and expect to close a second tranche by March 29, 2019.

January 28, 2019—Announced it has published a new study that further validates the stability of its proprietary test, ColonSentry®, as a tool to risk stratify patients who are non-compliant with any form of Colorectal Cancer screening and prioritize patients who should be referred directly for colonoscopy versus other modalities for colorectal cancer screening.

Risks and Disclosures

This Executive Informational Overview® (EIO) has been prepared by StageZero Life Sciences Ltd ("StageZero" or "the Company") with the assistance of Crystal Research Associates, LLC ("CRA") based upon information provided by the Company. CRA has not independently verified such information. Some of the information in this EIO relates to future events or future business and financial performance. Such statements constitute forward-looking information within the meaning of the Private Securities Litigation Act of 1995. Such statements can only be predictions and the actual events or results may differ from those discussed due to the risks described in StageZero's statements on its financial and other reports filed from time to time.

The content of this report with respect to StageZero has been compiled primarily from information available to the public released by the Company through news releases, presentations, Annual Reports, and other filings. StageZero is solely responsible for the accuracy of this information. Information as to other companies has been prepared from publicly available information and has not been independently verified by StageZero or CRA. Certain summaries of activities and outcomes have been condensed to aid the reader in gaining a general understanding. CRA assumes no responsibility to update the information contained in this report. In addition, CRA has been compensated by the Company in cash of thirty-eight thousand five hundred U.S. dollars and three hundred thousand options for its services in creating this report and for updates.

Investors should carefully consider the risks and information about StageZero's business. Investors should not interpret the order in which considerations are presented in this or other filings as an indication of their relative importance. In addition, the risks and uncertainties overviewed herein are not the only risks that the Company faces. Additional risks and uncertainties not presently known to StageZero or that it currently believes to be immaterial may also adversely affect the Company's business. If any of such risks and uncertainties develops into an actual event, StageZero's business, financial condition, and results of operations could be materially and adversely affected, and the trading price of the Company's shares could decline.

This report is published solely for informational purposes and is not to be construed as an offer to sell or the solicitation of an offer to buy any security in any state. Past performance does not guarantee future performance. Additional information about StageZero as well as copies of this report, can be obtained in either a paper or electronic format by calling (855) 420-7140.

RISKS AND UNCERTAINTIES

StageZero operates in a high-risk industry and is subject to numerous risks and uncertainties that may have an adverse effect on its results of operations and financial condition. An investment in StageZero and its securities should be carefully considered in light of the risks described below and the current economic and market conditions. These risks are not the only ones faced by the Company. Additional risks that are not presently known to StageZero or that the Company currently believes are immaterial may also significantly impair its business, results of operations, and financial condition.

Capital requirements, financing, and going concern.

From inception to date, StageZero has had no significant independent sources of income except for nominal sales of its product and proceeds from various collaborations and has accumulated significant losses. While the Company has added to its commercial test menu and believes this will lead to an increase in its commercial sales, there can be no guarantee that this will occur or will grow to a level necessary to finance its business. StageZero's ability to operate profitably and generate positive cash flow in the future will be affected by a variety of factors, including the availability of additional capital to fund its operations and to form strategic partnerships to access marketing and distribution capabilities, its ability to penetrate the market with commercial products, and its ability to obtain reimbursement coverage for its tests.

For the foreseeable future, StageZero will continue to be financed from the proceeds of equity financings and, to the extent available, from debt. Revenues from sales of tests are inconsistent. There can be no assurance that revenues from these sources will be anything more than nominal in the near term or sufficient to fund the Company's operating costs. StageZero's ability to continue as a going concern is also contingent upon its ability to obtain additional sources of capital to finance operations in the future. Efforts will be required to obtain this additional capital, but there is no assurance that additional capital will be available on acceptable terms, if at all. Similarly, StageZero's revenue from sales is not sufficient to fund its operations. The Company's inability to obtain sufficient additional capital may have a material adverse effect on the business, results of operations, and/or financial condition. If additional financing is raised through the issuance of equity or convertible debt securities, the interests of the Company's shareholders may be diluted. The auditor's report issued with respect of the Company's 2018 annual consolidated financial statements contains an "Emphasis of Matter", which includes the following statement:

> "Without qualifying our opinion, the Company draws attention to Note 2 to the consolidated financial statements, which indicates that StageZero Limited incurred a loss of $3,943,920 during the year ended December 31, 2018 and, as at that date had an accumulated deficit of $93,603,002. These conditions, along with other matters set forth in Note 2, indicate the existence of a material uncertainty that may cast significant doubt about the Company's ability to continue as a going concern."

As a result, StageZero's consolidated financial statements for the year ended December 31, 2018 and for the three months ended March 31, 2019 contain a going concern note with respect to this uncertainty. Substantial doubt about its ability to continue as a going concern may materially and adversely affect the price of the Company's common shares, and it may be more difficult for StageZero to obtain financing. The going concern note in its consolidated financial statements may also adversely affect StageZero's relationships with current and future collaborators and investors, who may grow concerned about the Company's ability to meet its ongoing financial obligations. If potential collaborators decline to do business with StageZero or potential investors decline to participate in any future financings due to such concerns, the Company's ability to increase its financial resources may be limited.

On May 4, 2016, StageZero received a notice of default from HDL for missing two monthly payments under the terms of the Notes that were renegotiated in March 2016. On August 15, 2016, Richard Arrowsmith, as Liquidating Trustee of the HDL Liquidating Trust, filed a Complaint against the Company in the United States Bankruptcy Court, Eastern District of Virginia, Richmond Division. The parties entered into negotiations and on March 1, 2017 reached a settlement agreement pursuant to which the Company would pay the Liquidating Trust an aggregate settlement amount of $2,095,843, to be paid in a $25,000 upfront payment and monthly payments of $15,000 beginning March 1, 2017 to July 1, 2017, followed by monthly payments of $10,000 until the outstanding debt has been paid in full. The Bankruptcy Court approved the settlement agreement and, on April 27, 2017, the action against the Company was dismissed with prejudice by the Bankruptcy Court.

The Company was a defendant in an action brought by the Trustees for the Estate of Health Diagnostic Laboratory, Inc., bankrupt since June 2015. The Trustees claimed that the Company was liable to the Estate of HDL in the amount of $178,801 for laboratory services rendered by HDL. Since the Company had paid approximately $83,000 towards these costs, the claim was netted at $95,770. The Company's counterclaim against HDL for $139,789 was considered unsecured and was not offset. The case was settled for $58,000 in January 2019, payable $10,000 on signing the Settlement Agreement and $2,000 per month for 24 months. No interest accrues to the settlement.

StageZero has prepared its financial statements on a going concern basis, which contemplates the realization of assets and the satisfaction of liabilities and commitments in the normal course of business. The Company's consolidated financial statements do not include any adjustment to reflect the possible future effects on the recoverability and classification of assets or the amounts and classification of liabilities that may result from the outcome of this uncertainty.

No record of profit

The Company has incurred significant losses to date and there can be no assurance that its future business activities will be profitable. Since inception, StageZero has incurred costs to develop and enhance its technology, to develop and commercialize its products and services, to establish strategic relationships, to acquire complementary technologies, and to build administrative support systems. The Company has experienced negative operational cash flow to date. It has incurred losses from operations of $3.9 million for the year ended December 31, 2018, and $2.9 million for the year ended December 31, 2017 as well as $6.0 million for the 3 months ended March 31, 2019 and $0.5 million for the 3 months ended March 2018. StageZero's ability to operate profitably and generate positive cash flow in the future will be affected by a variety of factors, including its ability to generate revenue and its quarterly operating results, the pace at which it secures additional marketing partners and customers, its ability to further develop and test its technology on schedule and on budget, the intensity of the competition the Company experiences and the availability of additional capital to pursue its business plan, including the development of new services. The inability to generate sufficient funds from operations is having a materially adverse effect on the Company's business, results of operations, and financial condition.

Share price

StageZero is an emerging company and operates within the biotechnology, molecular diagnostic, and genomic biomarker industry. The Company may experience large fluctuations in its share price as is common to many public companies in the industry. Factors such as announcements relating to its science, products, patents, or clinical studies, or regulatory or reimbursement changes, as well as the trading of its shares by insiders may have an adverse effect on the share price. In addition, shares are currently lightly traded and have experienced substantial volatility in the past, often based on factors unrelated to the Company's performance. These factors include global economic developments and market perceptions of the attractiveness of certain industries. It may also include the limited extent of analytical coverage for its business if investment banks with research capabilities do not follow the Company's securities; the lessening in trading volume and general market interest in StageZero's securities, which may affect a holder's ability to trade significant numbers of its common shares; and the size of its public float, which may limit the ability of some institutions to invest in the Company's securities.

StageZero may consider issuing convertible debt or equity securities, which may rank prior to the common shares, in the future to fund potential acquisitions or investments, or for general corporate purposes. The Company's articles of amalgamation provide that StageZero has an unlimited number of non-voting preference shares, of voting special shares (entitling the holder to a dividend if and when declared by the Board in parity with the common shares and convertible into common shares), and of voting common shares that may be issued. If StageZero issues convertible debt or equity securities to raise additional funds, the Company's existing shareholders may experience dilution, and the new convertible debt or equity securities may have advantageous rights, preferences, and privileges when compared to those of the Company's existing shareholders. StageZero is unable to predict the future amount of such issuances or dilution.

Public markets regulators

On the basis of the Company's financial condition, in January 2016, the Toronto Stock Exchange (the TSX) placed StageZero (then called GeneNews) under remedial delisting review as the Company did not meet the TSX's requirements with respect to its working capital position and market capitalization. The Company requested to be provided additional time to regain compliance with the continued listing requirements of the TSX and was granted until June 17, 2016 to demonstrate compliance with these continued listing requirements.

In March 2016, the Ontario Securities Commission (the OSC) granted the Company a management cease trade order ("MCTO"), which precludes members of management, specifically James Howard-Tripp, Executive Chairman, and Leslie Auld, former Chief Financial Officer, from trading the Company's common shares until such time as the cease trade order is no longer in effect. The Company complied with the provisions of the alternative information guidelines found in sections 4.3 and 4.4 of National Policy 12-203 Cease Trade Orders for Continuous Disclosure Defaults for so long as it is delayed in filing the annual and quarterly financial statements and related MD&A, CEO

and CFO certificates and its' Annual Information Form. The Company filed its annual filings on May 27, 2016 and completed its March 31, 2016 quarterly filings on June 15, 2016.

On June 16, 2016, the TSX completed its Remedial Review Process and determined that the Company met the TSX's continued listing requirement. Additionally, on this date, the OSC lifted the MCTO on members of management of the Company. While the Company's financial position has improved since the public market regulators placed it on remedial delisting review and MCTOs were granted, there is no guarantee that the Company won't be subject to further reviews by them.

Other collaborations and strategic partnerships

In 2016, StageZero (then called GeneNews) entered into a collaboration agreement with JTS Health Partners, a leading national healthcare management consulting and professional services firm based in Atlanta, Georgia and with NueHealth, LLC, a privately owned company that delivers value-based healthcare solutions and connects patients directly to physicians through integrated provider networks (or IPNs) in the U.S. In 2017, the Company entered into an agreement with a large, multi-specialty physician group in the American Midwest for use of StageZero's diagnostic tests. The Company expected that these collaborations will accelerate adoption of its menu of proprietary cancer tests, including its lead ColonSentry® blood-test for assessing an individual's current risk for colorectal cancer. With respect to StageZero's arrangement with JTS Health Partners, the Company expects that both parties will work to pursue and secure multi-year agreements for the Company's tests with hospitals, clinical integrated networks, physician groups, and healthcare organizations. With respect to its arrangements with NueHealth, LLC and with the Midwest multi-specialty physician group, the Company expects their physicians to adopt its test menu on a contracted basis. Should these initiatives fail to materialize in a timely manner or to generate sufficient revenue, StageZero's ability to continue operations and pursue its objectives may be adversely affected.

The Company has entered into license or other agreements in order to sell diagnostic tests developed by third parties that have been added to the Company's menu of tests and may do so in the future. These agreements include ones that are nonexclusive, short-term, or subject to termination on notice and that require minimum license or other payments to be made by the Company. As a result, these arrangements may terminate earlier than desired or result in fewer sales and lower revenues than expected.

The success of any license arrangement to sell a diagnostic test developed by a third party will be, in part, dependent on the financial health and reputation of the licensor and the intellectual property associated with the products and tests licensed to the Company. StageZero has also entered into a number of agreements and alliances with corporate, academic, hospital, and physician collaborators. These collaborations are typical in the Industry. The Company is highly reliant on such alliances to facilitate its research and development and commercialization programs. As an example, access to patient samples for research is essential to StageZero's continuing research. Although beneficial to the Company, these collaborations may expose it to additional risks. Should current collaborations and new alliances prove difficult or impossible to maintain, StageZero may be adversely affected.

Markets and competition

The industry in which StageZero operates is subject to rapid technological change, which may significantly alter the marketplace or result in changes in the regulatory and legislative environment. The Company's ability to successfully commercialize products or processes for diagnosing and managing colorectal cancer, lung cancer, prostate cancer, breast cancer, and other diseases in its development pipeline may depend, in part, on future market conditions, which are not possible to predict. The industry is populated with larger and more sophisticated companies whose financial and human resources far outweigh StageZero's. Any one or several of these competitors could announce findings or competitive approaches or products at any time, which could diminish or even eliminate competitive advantages currently held by StageZero.

The failure to adapt to any of the factors noted above could have a material adverse effect on StageZero's business, results of operations, and financial condition. Healthcare reform and controls on healthcare spending may limit the price charged for any of the Company's products or the amounts that can be sold. In particular, in the U.S., the federal government and private insurers have changed the manner in which healthcare services are provided and reimbursed. Potential approaches and changes in recent years include controls on healthcare spending, the creation of large purchasing groups and revisions to the methodology that Medicare uses for payment of laboratory tests. In the future, the U.S. government may institute further controls and different reimbursement schemes and limits on Medicare and Medicaid spending or reimbursement. These controls, reimbursement schemes, and limits might affect the revenues the Company could collect from sales of any products in the U.S. Uncertainties regarding future healthcare reform and private market practices could adversely affect StageZero's ability to sell any products profitably in the U.S. Election of new or different government officials in large market countries could lead to dramatic changes in pricing, regulatory approval legislation, and reimbursement, which could have material impacts on product approvals and commercialization.

Commercialization

Successful commercialization of StageZero's products will depend on a number of factors, including successful commercialization by the Company as well as its ability to:

- raise sufficient capital to fund current and future commercialization efforts;
- build a commercial team and supporting organizational infrastructure;
- establish partnerships and alliances with third parties to secure commercial capabilities that StageZero may not wish to build;
- market and distribute the Company's products;
- distinguish its products from others available on the market;
- obtain any necessary regulatory approvals for StageZero's facilities, products, and processes;
- gain reimbursement by third-party payers, such as private health insurers, managed-health organizations, and state-sponsored health insurance plans for each jurisdiction in which the Company's products are offered;
- educate physicians and change physician behavior to secure clinical adoption of StageZero's products;
- promote awareness of its products to increase market penetration;
- the ability to penetrate non-traditional revenue streams including, but not limited to, self-funded entities and self-insured organizations/associations, and
- publish in peer-reviewed journals.

There is no assurance that StageZero will be successful in these areas.

The Company believes that there may be different applications for products successfully derived from its technologies and that the anticipated market for products under development will continue to expand. StageZero cannot give assurance, however, that these beliefs will prove to be correct—the commercial viability of its products is yet to be established and the Company faces competition from existing or new products. Physicians, patients, third-party payers, or the medical community in general may not accept or use any products that StageZero or its collaborative partners may develop or in-license. Successful commercialization of ColonSentry® tests in the U.S. depends, in large part, on the availability of adequate reimbursement from public and private insurance plans.

In part, StageZero believes that obtaining a positive coverage decision and a favorable reimbursement rate from the Centers for Medicare and Medicaid Services (CMS) or their contractors may be a necessary element in achieving material commercial success. The US Preventive Services Task Force (USPSTF) is an independent, volunteer panel of national experts in prevention and evidence-based medicine, which makes recommendations about clinical preventative services, such as screenings, counseling services, and preventive medications. With the passage of the Medicare Improvement for Patients and Providers Act of 2008, Congress allowed the US Department of Health and Human Services (HHS) to authorize Medicare coverage for services rated A or B by the USPSTF. The USPSTF issued an update to the colorectal cancer screening guidelines in 2016. The USPSTF recommends screening for colorectal cancer in adults starting at age 50 and continuing until age 75 years and advises that the risks and benefits of different screening methods vary. ColonSentry® has not been evaluated by the USPSTF as a screening method.

Third-party payers are increasingly attempting to contain healthcare costs by limiting both coverage and the level of reimbursement for new healthcare products. As a result, there is significant uncertainty as to whether the use of tests that incorporate new technology, such as ColonSentry®, will be eligible for coverage by third-party payers or, if eligible for coverage, what the reimbursement rates will be for those products. If StageZero is unable to obtain positive coverage decisions from third-party payers or favorable rates of reimbursement for ColonSentry® tests at adequate levels, the commercial success of ColonSentry® technology would be constrained, and associated U.S. revenues would be significantly limited.

Regulatory authorizations

The Industry is highly regulated. Ultimate commercial success may depend on the Company's ongoing ability (whether directly or through IDL or other vehicles) to obtain the necessary regulatory authorizations for facilities, products, and processes. In addition, the process of obtaining regulatory authorization from governmental authorities to commercialize StageZero's products varies from country to country and by types of products and testing services. Depending on the circumstances, the process can be costly and time consuming, with ensuing delays in commercialization of a product or service. Regulatory authorization may be granted in part only or may be refused, which would negatively affect sales and profitability. In the U.S., medical devices, including screening tests, are subject to extensive regulation by the U.S. Food and Drug Administration (FDA) under the federal Food, Drug, and Cosmetic Act (FD&C Act) and its implementing regulations and by other federal and state statutes and regulations. The laws and regulations govern, among other things, medical device development, testing, labeling, storage, premarket clearance or approval, advertising and promotion, and product sales and distribution.

To be commercially distributed in the United States, medical devices must receive from the FDA either clearance of a premarket notification (510(k)) or a premarket approval (PMA) pursuant to the FD&C Act prior to marketing, unless subject to an exemption. Devices deemed to pose relatively less risk are placed in either Class I or II. Many Class I devices and some Class II devices are exempt from 510(k) premarket clearance. Those devices exempt from FDA premarket review must nonetheless comply with postmarket "general controls," unless the FDA has chosen to exercise "enforcement discretion" and not regulate them. Devices deemed by the FDA to pose the greatest risk are placed in Class III, requiring a PMA. The PMA pathway is costly, lengthy, and uncertain. The PMA review process typically takes one to three years but can take longer. The FDA's 510(k) clearance pathway usually takes from three to twelve months, but it can last longer, particularly for a novel type of product.

ColonSentry® is currently regulated as a laboratory developed test (LDT) in the U.S. under the clinical laboratory improvement amendments (CLIA) as well as applicable state laws. Generally, tests that are designed, developed, validated, and used within a single laboratory have been considered to be LDTs. The FDA has exercised enforcement discretion with respect to LDTs. On October 3, 2014, the FDA issued two draft guidance documents regarding oversight of LDTs. According to the draft guidance, the FDA intends to begin regulating LDTs using a risk-based, phased-in approach, in combination with continued exercise of enforcement discretion for certain regulatory requirements and certain types of LDTs. According to the draft guidance, all laboratories with LDTs—except for those only performing forensic testing or certain LDTs for transplantation—would need to comply with some basic statutory device requirements, regardless of the risks of the test, including adverse event reporting, corrections and removals reporting, and registration and listing or notification.

In addition, tests defined as high or moderate risk that are not subject to an exemption would need to be the subject of a PMA or 510(k) that is submitted to the FDA in a phased-in manner. The draft guidance has been the subject of considerable controversy, and it is unclear whether the proposed oversight regulations will be finalized, and if so, what they will contain. In addition, the U.S. Congress may act to provide further direction to the FDA on the regulation of LDTs. To date, it is unclear as to whether the FDA will finalize this guidance.

Even if required regulatory authorizations are obtained for StageZero's products, the Company will be subject to ongoing government regulation. As well, the manufacture, marketing, and sale of its products will be subject to strict and ongoing regulation. After a device, including a device exempt from FDA premarket review, is placed on the market in the U.S., numerous regulatory requirements apply. These include the quality system regulation (which imposes elaborate testing, control, documentation, and other quality assurance procedures), labeling regulations, registration and listing regulations, the medical device reporting regulation (which requires that manufacturers report to the FDA if their device may have caused or contributed to a death or serious injury or malfunctioned in a way that would likely cause or contribute to a death or serious injury if it were to recur), and the reports of corrections and removals regulation (which requires manufacturers to report recalls and field actions to the FDA if initiated to reduce a risk to health posed by the device or to remedy a violation of the FD&C Act).

Compliance with such regulations may be costly and may consume substantial financial and management resources. If StageZero or any marketing collaborators fail to comply with applicable regulatory requirements, it may be subject to sanctions, including fines, product recalls, or seizures; injunctions; total or partial suspension of production; civil penalties; withdrawal of regulatory authorizations; or criminal prosecution. Any of these sanctions could delay or prevent the promotion, marketing, or sale of its products.

Reimbursement

If StageZero, IDL, or the Company's marketing partners cannot obtain acceptable prices or adequate reimbursement for its products, StageZero's ability to generate revenues will be significantly diminished. The Company's ability to successfully commercialize products will depend significantly on the ability to obtain acceptable prices and the availability of reimbursement to the patient from third-party payers, such as government and private insurance plans. These third-party payers frequently require companies to provide predetermined discounts from list prices, and they are increasingly challenging the prices charged for medical products, including laboratory tests. StageZero's products may not be considered cost-effective, and reimbursement to the patient may not be available or sufficient to allow the Company to sell its products on a competitive basis. StageZero and its marketing partners may not be able to negotiate favorable reimbursement rates for the Company's products.

In addition, the continuing efforts of third-party payers to contain or reduce the costs of healthcare through various means may limit the Company's commercial opportunity and reduce any associated revenue and profits. StageZero expects proposals to implement similar government control to continue. In addition, increasing emphasis on managed care will continue to put pressure on the pricing of medical and healthcare products. Cost control initiatives could decrease the price that StageZero or any current or potential collaborators could receive for any products and could adversely affect its profitability. In addition, in the U.S. and many other countries, changes to reimbursement policies and rules may affect the reimbursement of its products. If StageZero fails to obtain acceptable prices or an adequate level of reimbursement for its products, the demand for products and their sales would be adversely affected or there may not be a commercially viable market.

Legal claims and regulatory proceedings

The Company may be involved from time to time in various legal claims and regulatory proceedings arising in the ordinary course of business, including arbitrations, class actions, civil litigation, and investigations. These matters may include but are not limited to intellectual property disputes; professional liability; employee-related matters and inquiries, including subpoenas and other civil investigative demands from governmental bodies; and Medicare, Medicaid or managed-care payer review of billing practices or requests for comment on allegations of billing irregularities that are brought to their attention through billing audits or third parties. Such inquiries may relate to the Company or to other healthcare providers.

The company operates in the clinical laboratory testing industry and therefore may be named in the future in suits brought under the qui tam provisions (whistleblower provisions) of the United States False Claims Act and comparable state laws. Suits under these provisions typically allege that an entity has made false statements and/or certifications in connection with claims for payment from federal or state healthcare programs. The suits may remain under seal (hence, unknown to the Company) for some time while the government decides whether to intervene on behalf of the qui tam plaintiff. Such claims are an inevitable part of doing business in the healthcare field today.

StageZero believes that the Company follows all material with respect to all statutes, regulations, and other requirements applicable to its operations. The clinical laboratory testing industry is, however, subject to extensive regulation with respect to sales and billing practices, quality control, and privacy of health information; many of these statutes and regulations have not yet been interpreted by the courts. There can be no assurance that those applicable statutes and regulations will not be interpreted or applied by a prosecutorial, regulatory, or judicial authority in a manner that would adversely affect the Company. Potential sanctions for violation of these statutes and regulations include significant fines and the loss of various licenses, certificates, and authorizations, which are critical to the Company's business. Such actions could also result in damage to StageZero's reputation and adversely affect its relationships with third parties.

Compliance with privacy laws

The Company is subject to privacy and security regulations in the U.S. with respect to the use and disclosure of protected health information. Subject to limited exceptions, the regulations restrict the Company's ability to use or disclose patient identifiable information without patient consent for purposes other than payment, treatment, or healthcare operations. There are significant fines or penalties for noncompliance with these requirements. In addition, any breach of the Company's security systems that results in personal information being obtained by unauthorized persons could adversely affect the reputation of the Company.

Ability to manage corporate growth, commercial expansion, and interruptions of operations

Responding to consumer demands, expansion into other geographical markets, and targeted growth in StageZero's business has placed and is likely to continue to place significant strains on the Company's administrative and operational resources and its internal systems, procedures, and controls. If the Company experiences rapid acceptance of its tests, the need to manage such growth will add to the demands on its management, resources, systems, procedures, and controls. There can be no assurance that StageZero's administrative infrastructure, systems, procedures, and controls will be adequate to support its operations, or that its officers and personnel will be able to manage any significant expansion of operations. If StageZero is unable to manage growth effectively, its business, financial condition, and results of operations could be materially adversely affected.

StageZero also depends on the efficient and uninterrupted operation of its single laboratory and computer and communications software, computer hardware systems, and other information technology, all located in Richmond, Virginia. The Company's activities and performance could cease or suffer if the laboratory or these systems were to fail or if StageZero were unable to successfully expand their capacity when necessary. Research and processes used by the Company and its partners require the use of sophisticated equipment, which may require a significant amount of time to obtain and install.

Although StageZero endeavors to properly maintain its equipment through proper service contracts and an inventory of key spare parts on hand, its activities could suffer if certain equipment or all or a portion of its facilities were to become inoperable for a period of time. This could occur for a variety of reasons, including catastrophic events such as weather-related damage, massive power failures, equipment failures, and/or delays in obtaining components or replacements, construction delays, or defects and other events that may be outside its control. Such a situation would result in a material adverse effect on StageZero's business, reputation, financial condition, and results of operation.

Key personnel

StageZero relies on certain key personnel for the management and development of its businesses. The experience, knowledge, and contributions of the Company's existing management team and its directors are and will continue to be important for the foreseeable future. As such, the loss of services from or retirement of such key personnel could have a material adverse effect on StageZero. In addition, the Company expects to be seeking additional full-time employees to increase its in-house capability to manage and operate its lab. There is competition for qualified personnel and there can be no assurance that StageZero will be able to attract and retain such personnel necessary for its businesses.

Foreign exchange rate risk

StageZero operates in Canada and the U.S. and transacts business primarily with U.S. partners and suppliers. The Company's functional currency is the USD. During the three-month period ended March 31, 2019, a 5% appreciation (depreciation) in the Cdn$ to U.S. dollar foreign exchange rate, with all else being equal, would have affected net income by approximately $265,000 [2018–$21,000]. The Company's exposure to foreign currency changes for all other currencies is not material.

Interest rate risk

Interest rate risk is the risk that the fair value or future cash flows of a financial instrument will fluctuate because of changes in market interest rates. The interest rate for the Company's notes payable to HDL was renegotiated during the first quarter of 2016 and interest began to be accrued at Wall Street Journal Prime Rate plus 4.00% per annum effective April 1, 2016, while the note payable to a shareholder and director as was issued in 2016 is fixed at 2% per annum, the note payable to shareholders and director as was issued in 2018 is fixed at 5% per annum, and the convertible debentures are fixed at 8%. Accordingly, there have been no significant impacts on the Company's consolidated statements of loss and comprehensive loss from changes in interest rates.

Licensee in the event of bankruptcy of a licensor

Rather than owning all of the intellectual property on which it relies, the Company licenses certain intellectual property and is substantially dependent on such licenses in order to market and sell such products. In the event that the licensor of any license the Company holds files a petition in bankruptcy, there can be no assurance that the rights under the Company's licenses will not be curtailed or otherwise affected, even if the company actively pursues enforcement of the license agreement. If a licensor files for bankruptcy, among other results, the licensed intellectual property may be sold to a third party and such sale may extinguish the Company's rights under any existing license agreements. This could cause a significant hardship for the Company as the licensee and have a material adverse effect on its business.

Material weakness in financial controls

In connection with the preparation of financial statements for the years ended December 31, 2018 and 2017, management identified material weaknesses in the internal controls over financial reporting. A material weakness of an issuer is defined as a deficiency or a combination of deficiencies in internal control over financial reporting such that there is a reasonable possibility that a material misstatement of its annual or interim financial statements would not be prevented or detected on a timely basis.

The material weaknesses pertained to ineffective controls in the financial statement close process and to ineffective oversight of the financial record keeping and reporting. This was as a result of not having sufficient accounting resources with relevant technical accounting skills to effectively and accurately prepare and review financial statements prior to finalization. Since identifying the weaknesses, StageZero has begun to remedy their respective material weaknesses through the continued development and implementation of formal policies, improved processes, and documented procedures, as well as the continued sourcing of additional qualified finance resources. The decline in revenues and the delay in obtaining sufficient external financing have had negative impacts on the timely resolution of these material weaknesses.

Although the Company is working on remedying the weakness as quickly as possible, it cannot at this time estimate how long it will take, and the initiatives may not prove to be successful in remedying the material weakness. If the remedial measures are insufficient to address these material weaknesses or if further significant deficiencies or material weaknesses in internal control over financial reporting are discovered or occur in the future, managements' ability to evaluate the financial reporting may be adversely affected. This would affect certifications, when required, regarding the effectiveness of its internal controls over financial reporting required by National Instrument 52-109 – Certification of Disclosure in the Company's annual and interim filings. In addition, if StageZero is not able to successfully remedy the material weakness, and if as a result is unable to produce accurate and timely financial statements or is required to restate its financial results, the Company's stock price may be adversely affected.

Litigation

Patent litigation is costly and time consuming and may subject the Company to liabilities. StageZero's involvement in any patent litigation, interference, opposition, or other administrative proceedings will likely cause it to incur substantial expenses, and the efforts of its key personnel will be significantly diverted. In addition, an adverse determination in litigation could subject StageZero to significant liabilities. Securities legislation in Canada has changed to make it easier for shareholders to sue. These changes could lead to frivolous lawsuits, which could take substantial time, money, resources, and attention, or could force the Company to settle such claims rather than seek adequate judicial remedy or dismissal of such claims.

Fluctuation in quarterly results

StageZero expects its quarterly operating results to fluctuate as a result of many factors, including the Company's ability to generate revenue, changes in the demand for its technology, the introduction of competing technologies, market acceptance of such enhancements or services, delays in the introduction of such enhancements or services, changes in the Company's pricing policies or those of its competitors, the ability of the Company to obtain reimbursement for tests and the time to collect these amounts, the mix of services sold, foreign currency exchange rates, and general economic conditions.

Glossary

5-year Survival—The percentage of people in a study or treatment group who are alive five years after they were diagnosed with or started treatment for a disease, such as cancer.

AUROC (area under the ROC curve)—A receiver operating characteristic curve, or ROC curve, is a graphical plot that illustrates the diagnostic ability of a system, by determining how any predictive model can distinguish between the true positives and negatives. The ROC curve can determine how well the presence of a biomarker can predict disease status. The AUROC is a performance measure, with higher numbers reflecting a better model at distinguishing between patients with disease and no disease.

Assays—The investigative procedure (and the substance used) for qualitatively assessing or quantitatively measuring the presence, amount, or functional activity of a target entity (the analyte).

Autoantibodies—Antibodies (immune proteins) that target and react with a person's own tissues or organs. Autoantibodies may be produced by a person's immune system when it fails to distinguish between "self" and "non-self" and are the cause of some autoimmune diseases.

Benign Prostatic Hyperplasia (BPH)—A common, noncancerous enlargement of the prostate gland. The enlarged prostate may compress the urinary tube (urethra), impeding the flow of urine from the bladder.

Biomarkers—A measurable substance in an organism whose presence is indicative of some phenomenon such as disease, infection, or environmental exposure**.**

College of American Pathologists (CAP)—A member-based physician organization comprising of approximately 18,000 board-certified pathologists. The CAP provides accreditation and proficiency testing to medical laboratories through its laboratory quality solutions programs.

The Clinical Laboratory Improvement Amendments (CLIA)—A U.S. federal regulatory standards that regulates laboratory testing and require clinical laboratories to be certificated by their state as well as the Center for Medicare and Medicaid Services (CMS) before they can accept human samples for diagnostic testing.

Colonoscopy—A procedure in which a flexible fiber-optic instrument is inserted through the anus in order to examine the colon.

Concierge Physicians—A relationship between a patient and a primary care physician in which the patient pays an annual or monthly fee in exchange for enhanced access and personal attention, in addition to regular charges.

Cytoplasm—The material within a living cell, excluding the nucleus.

Enzyme-linked Immunosorbent Assay (ELISA)—A biochemical procedure in which a signal produced by an enzymatic reaction is used to detect and quantify the amount of a specific substance in a solution.

Exosomes—Best defined as extracellular vesicles that are released from cells upon fusion of an intermediate endocytic compartment, the multivesicular body (MVB), with the plasma membrane.

False Negative—A test result which incorrectly indicates that a particular condition is absent when in reality it is present. A false negative could result in a patient with a particular condition or disease given a clean bill of health.

False-Positive—A test result which incorrectly indicates that a particular condition or attribute is present. A false positive could result in a patient being incorrectly told they have the particular disease.

Fecal Occult Blood Testing (FOBT)—A lab test used to check stool samples for hidden (occult) blood. Occult blood in the stool may indicate colon cancer or polyps in the colon or rectum.

Free PSA—PSA, a protein produced by prostate gland cells, circulates through the body in two ways: either bound to other proteins or on its own. Free PSA is the PSA that is floating freely in the bloodstream, without being bound to a different protein. *See Prostate Specific Antigen (PSA) in the glossary.*

Gene Expression—Gene expression is the process by which information from the DNA in a gene is used in the synthesis of a functional product. Genes can be expressed as either RNA or protein.

Interval Cancers—A cancer that develops in the intervals between routine screening.

Liquid Biopsy—A test done on a sample of blood to look for cancer cells from a tumor or for pieces of DNA from tumor cells that are in the blood. A liquid biopsy may be used to help find cancer at an early stage. It may also be used to help plan treatment or to find out how well treatment is working or if cancer has come back.

Low Dose Computed Tomography (LDCT)—Computed tomography (CT) scanning combines special x-ray equipment with sophisticated computers to produce multiple, cross-sectional images or pictures of the inside of the body. LDCT uses less ionizing radiation than a conventional CT scan. Since this a radiographic technique can provide high-quality, 3-D images of the lungs, it is used for screening asymptomatic, high-risk individuals for early lung cancer lesions.

Messenger RNA (mRNA)—A subtype of RNA in which a portion of genetic information transcribed from DNA is carried to other parts of the cell for protein synthesis processing. *See ribonucleic acid in the glossary.*

Negative Predictive Value—The probability that subjects with a negative screening test truly do not have the disease.

Overdiagnosis—The diagnosis of a disease that will never cause symptoms or death during a patient's ordinarily expected lifetime. Overdiagnosis is a side effect of screening for early forms of disease, and occurs when a disease is diagnosed correctly, but the diagnosis is irrelevant.

PAP (Papanicolaou) Test—A screening procedure in which a small brush or spatula is used to gently remove cells from the cervix so they can be checked under a microscope for cervical cancer.

pro2 PSA—Pro-PSA is a molecular form of free PSA, a protein that is associated with cancer and can further increase the specificity for prostate cancer tests. In particular, pro2 PSA, a truncated form of pro-PSA, may be a useful marker for the detection of prostate cancer. *See Free PSA in the glossary.*

Proenkephalin (pro-ENK)—An opiate neuropeptide precursor gene, they encode enkephalins, a peptide involved in regulating nociception in the body (the sensory nervous system's response to certain harmful or potentially harmful stimuli) by binding to the body's opioid receptors.

Proneurotensin (pro-NT)—An endogenous neuropeptide, it is the precursor of neurotensin, a hormone that regulates both satiety and breast cancer growth.

Prostate Specific Antigen (PSA)—A protein produced by prostate gland cells, which circulates through the body in two ways: either bound to other proteins or on its own. A test for PSA, which measures the total of both free and bound PSA, may be used to screen for cancer of the prostate and to monitor treatment of the disease.

Regression-based Algorithm—An algorithm that predicts new output values or outcomes created based on existing data. By using regression algorithm methodology, a model is built that fits the available data and that can predict outcomes for new data.

Ribonucleic Acid (RNA)—A nucleic acid present in all living cells. Its principal role is to act as a messenger carrying instructions from DNA for controlling the synthesis of proteins.

Risk Stratification—A tool for identifying and predicting which patients are at high or elevated risk of developing a particular disease, in order to prioritize and provide direction for the management of their care.

Sensitivity—Also called true positive rate, measures the proportion of actual positives that are correctly identified as such, or how often a test correctly generates a positive result for people who have the condition that's being tested for. Low sensitivity leads to *false negative.*

Specificity—Also called true negative rate, measures the proportion of actual negatives that are correctly identified as such (e.g., the percentage of healthy people who are correctly identified as not having the condition). Low specificity leads to false positive, where a person is incorrectly told they have the particular disease.

Sigmoidoscopy—A test used to check the inner lining of a person's rectum and lower part of the colon**.**

Telehealth—Also called telemedicine, telehealth is the use of electronic information and telecommunications technologies to support and promote long-distance clinical health care, patient and professional health-related education, public health, and health administration.

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