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Bluejay Diagnostics, Inc. (BJDX: NASDAQ)

BJDX: Orchestrating a New Testing Standard

We employ a discounted cash flow (DCF) model and a 15% discount rate in our valuation of Bluejay Diagnostics. Our methodology applies a 50% probability of commercial success to Bluejay's Symphony Platform.

Current Price (5/30/2023)	$0.19
Valuation	**$2.00**

INITIATION

Bluejay Diagnostics is developing the Symphony™ diagnostic testing system which is able to rapidly detect IL-6 in emergent care settings in whole blood for patient triage. IL-6 is an important early detection marker for sepsis, cancer progression, rheumatoid arthritis, COVID and other severe conditions. It is a clinically established biomarker for assessment of severity of infection and inflammation across many disease indications.

The device was evaluated in a 2016 study. It found a high positive correlation between the Symphony system and the CLEIA standard supporting its use in identifying RA patients in need of emergent treatment. A 2021 study found it comparable with an EUA cleared product for COVID triage.

Bluejay is now investigating the test in the clinic for sepsis triage and monitoring. Other earlier stage programs for hsTNT/I and NT-proBNP for MI and heart failure are also proposed on the Symphony platform.

The NIH estimates ~1.7 million US cases of sepsis per year and 270,000 related deaths. Other indications with higher prevalence could also benefit from rapid IL-6 detection.

If Bluejay obtains regulatory approval for IL-6 sepsis triage and monitoring, it will pursue additional diagnostic tests for MI, CHF, neutropenic sepsis in cancer & other disease indications.

SUMMARY DATA

52-Week High	**1.83**
52-Week Low	**0.19**
One-Year Return (%)	**-92.2**
Beta	**0.84**
Average Daily Volume (sh)	**210,080**
Shares Outstanding (mil)	**20.5**
Market Capitalization ($mil)	**4.0**
Short Interest Ratio (days)	**0.4**
Institutional Ownership (%)	**1.4**
Insider Ownership (%)	**44.6**
Annual Cash Dividend	**$0.00**
Dividend Yield (%)	**0.00**
5-Yr. Historical Growth Rates	
Sales (%)	**N/A**
Earnings Per Share (%)	**N/A**
Dividend (%)	**N/A**
P/E using TTM EPS	**N/A**
P/E using 2023 Estimate	**N/A**
P/E using 2024 Estimate	**N/A**
Zacks Rank	**N/A**

Risk Level	**Above Average**
Type of Stock	**Small-Growth**
Industry	**Med-Tech/Devices**

ZACKS ESTIMATES

Revenue

(In millions of USD)

	Q1 (Mar)	Q2 (Jun)	Q3 (Sep)	Q4 (Dec)	Year (Dec)
2022	$0.0 A	$0.2 A	$0.0 A	$0.0 A	$0.2 E
2023	$0.0 A	$0.0 E	$0.0 E	$0.0 E	$0.0 E
2024					$0.0 E
2025					$1.6 E

Earnings per Share

	Q1	Q2	Q3	Q4	Year
2022	-$0.10 A	-$0.10 A	-$0.15 A	-$0.12 A	-$0.46 A
2023	-$0.12 E	-$0.07 E	-$0.04 E	-$0.04 E	-$0.24 E
2024					-$0.17 E
2025					-$0.16 E

INITIATING COVERAGE

We are initiating coverage of Bluejay Diagnostics, Inc. (NASDAQ: BJDX) assigning a valuation of $2.00 per share. Bluejay is a diagnostic device development company offering its Symphony product pipeline. The company is advancing a sepsis triage and monitoring system for intensive care unit (ICU), emergency room (ER) and other hospital settings where accurate and rapid results are critical. Symphony is an on-site, rapid turnaround immunoanalyzer that is able to provide results in less than 20 minutes. This is in contrast to the existing approach that relies upon analysis by offsite labs which can take a day or more to return results.

Sepsis is the leading cause of mortality in hospitals contributing to 20% of deaths globally.[1] It is also one of the costliest causes, with an estimated $62 billion expenditure at inpatient facilities for related treatment in 2019 according to Medicare data. Early treatment is necessary to prevent death and improve recovery. Time is of the essence and a patient can convert from stable to critical condition in just a few hours. Interleukin-6 (IL-6) is a timely and proven biomarker that is a potent indicator of sepsis or septic shock. Blood levels of IL-6 above a certain threshold may predict a fatal outcome. Despite the utility of the IL-6 biomarker, there is no consistent and timely measure of the cytokine, especially in emergency room (ER), intensive care unit (ICU) and long-term acute care (LTAC) facilities where sepsis frequently occurs. In most cases, tests for IL-6 must be sent to a central lab where it can take hours to days to get a reading, and results can arrive after critical decisions must be made.

Hospital labs are geared towards high volume tests and when a new analyte is prepared to be measured, calibration must take place and new reagents must be added. While most laboratory analyzers are able to generate a result in under an hour, there are additional time-consuming steps beforehand that extend the process in many cases beyond a day, including the queueing of sufficient tests to justify a run. Preliminary steps include:

- Transportation of whole blood to laboratory facility
- Centrifuge of whole blood into fractionated parts
- Calibration of and supplying reagents into analyzer

Bluejay's Symphony system can address these shortcomings by providing a mobile, on-site analyzer using whole blood and single-use calibrated cartridges that can generate a result in under 20 minutes.

Symphony is distinguished from other IL-6 testing methods in several respects compared with the existing standard:

- Able to produce a result in less than 20 minutes vs. 24 to 48 hours
- Uses 150 µL whole blood vs. greater volumes of centrifuged blood plasma
- Provides mobile access vs. transfer to off-site laboratory
- Economical alternative for low to medium volume tests vs. batching requirements in the lab
- Guides clinical decision making by identifying high risk patients

The availability of Symphony is expected to expand the use of IL-6 testing. Many of the critical conditions that benefit from an IL-6 reading are time-dependent and require a result within minutes to hours in order to guide emergent treatment.

The process for running a diagnostic test using Symphony requires 150 µL microliters of blood which is then fed into the Symphony IL-6 cartridge. The cartridge, along with as many as five others, is inserted into the Symphony diagnostic analyzer which is able to evaluate the sample in under 20 minutes. The testing process centrifuges the blood inside the cartridge and then analyzes it using reagents contained inside. The system employs sandwich-ELISA which generates fluorescence measured by a light emitting diode (LED) producing a result sensitive to within 3 picograms per milliliter.[2]

Two studies have been completed using the Symphony system. The first in 2016, was undertaken in Japan to measure IL-6 levels in rheumatoid arthritis (RA) patients. The rapid and accurate results were able to evaluate the severity and predict outcomes in trial subjects and show a tight correlation with existing chemiluminescent enzyme immunoassay (CLEIA) systems that are only appropriate to high test throughput settings. The second was a study

[1] Rudd, K.E. *et al*. Global, regional, and national sepsis incidence and mortality, 1990–2017: analysis for the Global Burden of Disease Study. The Lancet, January 18, 2020.
[2] Bluejay Diagnostics KOL Event. The Emerging Use of Biomarkers in Contemporary Management of COVID-19/Respiratory Failure. 26AUG22.

in COVID patients that assessed the prognostic accuracy in predicting patients at high risk of progressing to invasive mechanical ventilation. A poster presented on the study concluded that Symphony was able to produce laboratory quality results with a faster turnaround time using whole blood, near patient, with 98% negative predictive value.[3]

Clinical trials are underway at a number of sites throughout the United States. Bluejay is conducting an extension of its ongoing trial and will meet with the FDA to finalize trial endpoints and protocol. We expect Bluejay to use 28-day mortality as its primary endpoint to stratify patient risk. A pre-submission meeting will be held with the FDA, to seek an appropriate approval pathway that is expected to use procalcitonin as the predicate test using the 510(k)-approval process. If approval is granted, Bluejay expects to commercialize the Symphony product starting at the sites used for clinical trials by employing a small sales force. Distributors will also be used to expand the reach further. Bluejay has rights to the Symphony system licensed from the Japan-based Toray Industries in the United States and rest of world excluding Japan. We anticipate that Bluejay will begin to seek partners outside the US to commercialize the product following grant of marketing authorization domestically.

Testing for emergent conditions and triage of patients for IL-6 and other critical niche analytes is a dramatic unmet need that is negatively impacted by the need to use a central laboratory that requires batching, calibration and test runs before conducting measurements, usually for multiple samples from different patients and locations.

Bluejay held $6.8 million in cash as of March 31, 2023 which we expect will be sufficient to support operational activities for the balance of 2023. We expect that there will be an additional raise in the next 12 months to support operational activities as the anticipated 510(k) application is reviewed.

Key reasons to own Bluejay Diagnostics shares:

- **Symphony system offers several advantages over traditional systems**
  - **Ease of use**
  - **Cost, time and space savings**
  - **Versatile platform able to support a broad test menu**
  - **Throughput and multiple testing capability**
  - **Immediate test of analyte, which can degrade during wait in queue**
- **Bluejay holds global license (ex-Japan) for manufacturing, marketing and sale of Symphony system**
  - **Domestic commercialization using small sales force and distributors**
  - **Ex-US commercialization using partners and distributors**
- **Further expansion into additional low volume, quick turnaround tests**
  - **Chest pain markers**
  - **Autoimmune disease**
  - **Inflammatory diseases**

Bluejay will be pursuing an FDA marketing authorization for its Symphony IL-6 diagnostic test for use in sepsis triage following the completion of its active clinical trial. We anticipate further clinical work to develop hsTNT and NT-proBNP rapid turnaround for chest pain using the same cartridge system.

In this report we provide a description of the Symphony immuno-analyzer and the indications being pursued by Bluejay in sepsis and chest pain. A review of the 510(k) regulatory pathway is provided followed by a discussion of the IL-6 analyte, its importance as a biomarker and its advantages for use in sepsis triage. Further discussion examines the intellectual property that protects the cartridge and the licensing agreement between Bluejay and Toray Industries. Following sections summarize the risks faced by diagnostic and device companies and for Bluejay in particular. The research report summarizes the main peers and competitors providing diagnostic testing equipment and IL-6 tests in particular and the management team is introduced. Our closing sections provide a summary of key milestones over the recent past and a valuation of the company. The valuation section provides the assumptions behind our discounted cash flow (DCF) model that values the commercialization of the IL-6 test and generates a target price of $2.00 for Bluejay Diagnostics.

[3] In diagnostic testing, negative predictive value is a statistical measure that indicates the probability that a subject with a negative test result truly does not have the condition or disease being tested. It helps to determine the reliability of a negative test result in ruling out the presence of a particular condition.

Diagnostic Platform

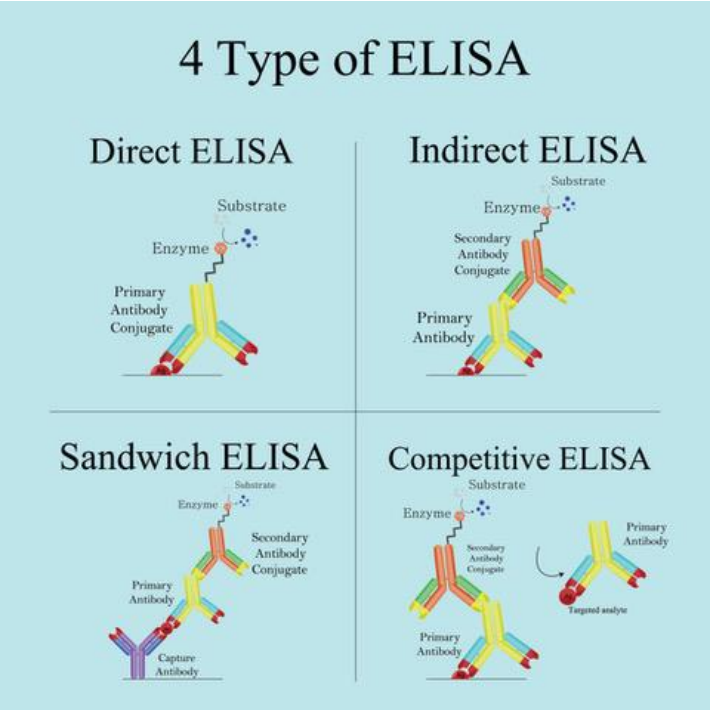
Symphony Immuno-analyzer Diagnostic System

Bluejay is advancing the Symphony Immuno-analyzer through the regulatory process in the United States with the ultimate goal of obtaining FDA marketing authorization to commercialize the product. It provides an innovative solution to rapidly analyze small quantities of blood and identify a number of analytes in a small, portable and relatively inexpensive device. It can provide laboratory quality analysis for a number of critical conditions that use interleukin-6 (IL-6) as a biomarker including COVID-19, sepsis, rheumatoid arthritis (RA) and cancer. Symphony does not require specialized training to operate, eliminating the need for trained, dedicated staff. Measuring IL-6 can serve as an early warning sign of a patient's prognosis and inform rapid and precise treatment.

The Symphony system was initially developed by Toray Industries, Inc., which began development in 2008. It has been using the product as a Research Use Only (RUO) product in Japan to monitor IL-6 in rheumatoid arthritis (RA) patients. The device uses the Enzyme-Linked Immunosorbent Assay (ELISA) method of testing and applies its patented cartridge that applies advanced nanotechnology and microfluidics.

Enzyme-Linked Immunosorbent Assay (ELISA)
The enzyme-linked immunosorbent assay (ELISA) is a commonly used analytical biochemistry assay used for serologic testing. The test is able to detect specific antibodies or antigens that may appear in the presence of disease. It is commonly used to identify the presence of human immunodeficiency virus (HIV), Lyme disease, COVID-19, squamous cell carcinoma, syphilis and many other diseases that are difficult to detect through other means.

Exhibit I – Types of ELISA[4]



The ELISA test is held as the gold standard in the industry[5] and can detect trace amounts of antibodies, antigens, proteins, glycoproteins and hormones. ELISA tests are frequently performed in chemical and heat resistant polystyrene receptacles, typically 96-well plates, coated to bind protein. The test may require either a primary and/or secondary detection antibody, analyte/antigen, coating antibody/antigen, buffer, wash, and substrate. The detection antibody or antigen only binds to the protein of interest. An enzyme-linked secondary antibody will then bind to the detection protein and will produce a color when exposed to a substrate to indicate that the protein of interest is present. Four types of ELISA tests are used and are designated direct, indirect, sandwich and competitive.

[4] Source: Shutterstock, Image 1888246531
[5] Alhajj, M., Farhana, A. Enzyme Linked Immunosorbent Assay. National Library of Medicine. February 2022.

The general process for running the ELISA test requires multi-well, microtiter plates where the wells of the plate are coated with the antigen of interest. The wells are then filled with the patient's serum and antibodies against the antigen will bind to the antigens, if present. The wells are then washed, then another solution with a second antibody that will bind to the first antibody is introduced. The second antibody is covalently bound to an enzyme that will produce a certain luminescent color when the substrate is added. The color can be seen or quantified with an electronic plate reader and its intensity changes with the titer of the measured substance.

In some cases, such as the one for the sandwich ELISA, which is the type used in the Symphony system, a surface is coated with an antibody which can bind to the antigen of interest. After a wash, a second antibody that is bound to an enzyme is added so that the test can produce a color indicating the presence of the antigen in the presence of the substrate.

Symphony System

Symphony is an automated diagnostic system, consisting of a fluorescence immuno-analyzer which uses a single-use diagnostic test cartridge with reagents integrated into the cartridge. The system uses a 'sample-to-result' format, which means that once a specimen is taken from the patient, it is placed in the cartridge and then the cartridge is placed inside the analyzer where the test is run without further technician intervention or use of additional reagent. This reduces test complexity and eliminates the need for highly trained and expensive laboratory technicians to run the tests. The platform is designed to enable simple, rapid, and cost-effective analysis from a single clinical sample, which will allow long-term acute care facilities (LTACs), hospitals and clinics that have not been able to afford more expensive or complex diagnostic testing platforms access to this tier of analysis. The device can provide better patient testing at an affordable cost in time sensitive, life-threatening situations. The system also allows for a faster turnaround given as the equipment is used in-house as compared to the traditional use of an off-site laboratory. On-site testing may also help support the decision-making process and help avoid potential penalties often imposed on LTACs by insurance companies and government programs for failure to monitor for potential sepsis.

Symphony System Components

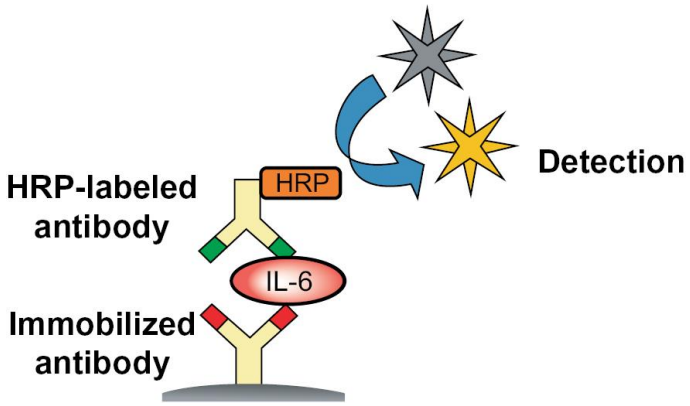
The Symphony system is comprised of two components: the Symphony Fluorescence Immuno-analyzer and the Symphony cartridge library. The analyzer conducts the whole blood processing, biomarker isolation and immune assay preparation using non-contact centrifugal force. The reagents and components required for testing are integrated into the cartridges. Whole blood is processed using precision microchannel technology and high specificity antibodies within the cartridge. Intermittent centrifugal cycles move analytes into various chambers that introduce reagents and stimulate reactions that produce the test result. When the test is complete, the analyzer measures the fluorescence signature and quantifies the biomarker.

Exhibit II – Symphony Fluorescence Immuno-analyzer and IL-6 Cartridge[6]

[6] Source: Bluejay Diagnostics management

The test operates on the same principle as sandwich ELISA tests, which we discuss above. The Symphony cartridge contains an assay that separates plasma from whole blood and forms complexes through the reaction of IL-6 with highly specific IL-6 binding antibodies. After the IL-6 sandwich is formed, a fluorescent substrate interacts with the enzyme and produces fluorescent molecules. The fluorescence intensity is measured and converted to IL-6 concentration. The entire process is performed within the Symphony IL-6 cartridge and is controlled and measured by the Symphony Fluorescence Immuno-analyzer.

Exhibit III – The Symphony Binding and Detection Process[7]



The Symphony Test Cartridge requires 150 µL (approximately three drops) of blood to produce a reading. A fill gauge is provided on the cartridge (see below to the right of the "High –" and "Low –" markings) to indicate sufficient volume of blood. To read the cartridge, patient data is entered and the cartridge is inserted into the Symphony analyzer and the test runs itself. Up to six cartridges can be inserted into the Symphony device at once which can measure either six different samples or biomarkers. In less than 20 minutes, the device generates the measurement results for review.

The cartridge contains all the reagents necessary to run the test, which is composed of three parts: sample preparation, chemical reaction and detection. All steps are performed in chambers inside the cartridge and byproducts of the test are retained inside the enclosure which reduces the risk of contamination.

Exhibit IV – Symphony IL-6 Cartridge[8]

The Symphony system was previously known as Ray-Fast when it was the subject of a study sponsored by Toray Industries. The 2016 study, conducted by Bluejay's licensor, evaluated the accuracy of the device to measure IL-6 levels in RA patients. Results from the study, also known as the Japan Study, were memorialized in a journal article published in Cytokine titled "Development of a quick serum IL-6 measuring system in rheumatoid arthritis."

[7] Source: Bluejay Diagnostics S-1 filing, October 2021.
[8] Source: Bluejay Diagnostics S-1 filing, October 2021.

In the Japan Study[9], the platform demonstrated its ability to provide laboratory quality results in an on-site format that provides compelling speed, accuracy and cost compared with existing alternatives. The system requires only a few hundred femtograms (10^{-10} grams) of the analyte to provide a reliable result. A result is available within 20 minutes of launching the test. New design improvements have shortened the time required to produce results and it is expected that future refinements will further reduce the duration. While the first efforts for Symphony will be to detect IL-6 in sepsis patients, the platform offers additional potential for other diagnostic tests.

Bluejay expects to follow the 510(k) pathway for Symphony's approval, which is a regulatory route for products that have a predicate device already legally marketed in the United States.

Manufacturing
Bluejay has an arrangement with partner Toray Industries, Inc. to manufacture cartridges and with Sanyoseiko Co., Ltd. to manufacture both devices and cartridges. Toray is headquartered in Tokyo, Japan and was established in 1926. It operates globally with almost 50,000 employees in several industries including life sciences, specifically pharmaceuticals and medical devices. Sanyoseiko was established in 1963 in Otsuki City in Japan to manufacture precision parts for optical products. As it moved through the decades towards today, it has obtained numerous licenses including several for manufacturing medical devices.

COVID Study
Bluejay presented clinical results for the Symphony IL-6 test at the American Association for Clinical Chemistry (AACC) 2022 in late July last year. Investigators from the University of Texas Southwestern (UTSW) Medical Center in Dallas, Texas, found the analytical and clinical performance of the Symphony IL-6 Test comparable to the Emergency Use Authorization (EUA)-approved Roche Elecsys IL-6 assay. The test is able to identify COVID patients at high risk for severe disease, including those that require mechanical ventilation. A poster entitled "Evaluation of a new, Near-Patient Testing (NPT) IL-6 Assay on Symphony Immunoanalyzer" was presented at AACC. It summarized the use of the Symphony system in the emergency department and intensive care unit setting.

Key features of the Symphony Device included in the presentation:

- Faster turnaround time of less than 20 minutes
- Ease of use which allows for the use of whole blood and does not require laboratory infrastructure
- Lack of other IL-6 near patient testing solutions
- Analytical precision
    - 98% negative predictive value, substantially better than other EUA approved devices
    - 89% sensitivity and 64% specificity
    - High correlation with gold standard Roche Test with r = 0.9490[10]

Exhibit V – Comparison of Symphony with Traditional IL-6 Tests[11]

	Symphony IL-6 Test	Traditional IL-6 Tests
Sample to Result	<20 minutes	>30 minutes
Sample/Processing	Whole Blood/None	Plasma/Required
Methodology/Reagents	ELISA/Fully integrated	ELISA/Separate
Maintenance	Minimal	Significant
Training	Simple	Complex
Waste	Contained in cartridge	Handling required
Size	Small	Large

[9] The Japan Study that is referred to throughout Bluejay's materials is cited here: Koyama, K., *et al*. Development of a quick serum IL-6 measuring system in rheumatoid arthritis. Cytokine, February 2017.
[10] The "r" value is the correlation coefficient, which indicates the direction and strength of the relationship between two variables, which in this case is the performance between the Symphony and the Roche Elecsys IL-6 assay.
[11] AACC Poster Presentation, Evaluation of a new, Near-Patient Testing (NPT) IL-6 Assay on Symphony Immunoanalyzer. K. Jaleta, N. Patel, M. Narasimhan, A. Muthukumar

Symphony was compared against the Roche Elecsys IL-6 assay which measured multiple blood and plasma samples. With regard to clinical performance, 147 COVID-19 patient samples were evaluated and the sensitivity and specificity of both assays were found to be comparable. The Symphony assay was relatively better for ruling out disease severity, whereas the Roche assay was slightly better for ruling in disease severity. The difference in the prevalence rate of disease severity may be the contributing factor for the variations seen in predictive values between the two assays.

Exhibit VI – Relative Accuracy for Symphony and Roche cobas IL-6[12]

IL-6 (pg/mL)	Symphony IL-6 assay (whole blood)			Roche cobas IL-6 assay (plasma)		
	# of patients on IMV	# of patients not on IMV		# of patients on IMV	# of patients not on IMV	
≥ 35	16	47	PPV=25%	16	11	PPV=59%
< 35	2	82	NPV=98%	3	19	NPV=86%
Sensitivity	89%			84%		
Specificity		64%			63%	
Prevalence		12%			39%	

*Invasive Mechanical Ventilation (IMV) *Positive Predictive Value (PPV) *Negative Predictive Value (NPV)

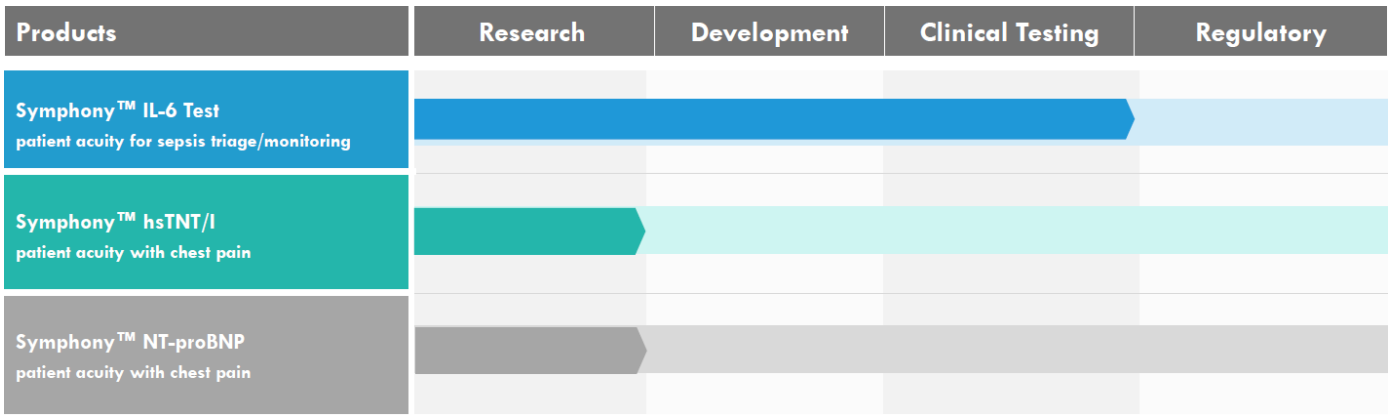
The poster concluded that the performance of the Symphony and cobas IL-6 assays were comparable. Symphony offered several advantages vs. its Emergency Use Authorization (EUA)-cleared competitor including smaller form factor, better cost-effectiveness, greater ease of use and faster turnaround time. These elements support its use in emergency and critical care settings to effectively triage COVID and other patients at risk of sepsis.

[12] AACC Poster Presentation, Evaluation of a new, Near-Patient Testing (NPT) IL-6 Assay on Symphony Immunoanalyzer. K. Jaleta, N. Patel, M. Narasimhan, A. Muthukumar

Indications

Bluejay Diagnostics' lead program is targeting sepsis triage using IL-6 as a marker. A chest pain triage using the markers hsTNT and NT-proBNP is in earlier stage development. The sepsis program is the furthest along and is undergoing pivotal studies that will provide the necessary data to support a 510(k) application. When clinical testing is complete, we anticipate that Bluejay will submit its package to the FDA in 2024. The chest pain program is also in development at the research stages. The category will measure the impact of two biomarkers, hsTNT/I and NT-proBNP, which are key to diagnosing heart attack and heart disease among other related conditions. They offer wide applicability and have been identified by specialists as the most important diagnostic biomarkers in an emergent setting.[13]

Exhibit VII – Bluejay Diagnostics Pipeline[14]



Sepsis[15,16,17,18,19]

Sepsis is a potentially life-threatening complication of an infection that occurs when the body's immune system overreacts and damages its own tissues and organs. It is a leading cause of death in hospitals worldwide, estimated to affect 1.7 million adults in the United States[20] and 47 to 50 million around the globe[21] each year. Over 20% fail to survive and patients that do survive are at greater risk of rehospitalization and death. Further, sepsis survivors suffer from persistent impairments such as cognitive deterioration, brain dysfunction, cardiovascular events and an increased chance of hospital readmission in the weeks to months after discharge. It is caused by a number of factors including viral or bacterial infection, pneumonia and blood poisoning among others.

Sepsis falls into two categories: sepsis and septic shock. Sepsis is both the general term for all stages and a systemic response to an infection, characterized by inflammation and organ dysfunction. Symptoms can include fever, increased heart rate, rapid breathing and decreased blood pressure. Septic shock presents a more advanced response that includes organ dysfunction and low blood pressure that requires vasopressor medications to maintain blood pressure. Both sepsis and septic shock are medical emergencies and require immediate attention. Septic shock can be fatal if not treated immediately. Septic shock is a severe circulatory, cellular and metabolic dysregulation that has higher mortality than sepsis.

Prevalence

In the United States, sepsis is estimated to occur in 1.7 million people each year according to the National Institute of Health (NIH) and is a leading cause of death among hospital patients, accounting for ~270,000 deaths annually. Around the globe, the World Health Organization (WHO) estimates that sepsis affects almost 50 million persons every year causing 11 million deaths and billions of dollars in healthcare costs.

[13] Bluejay Diagnostics S-1, filed October 4, 2021.
[14] Source: Bluejay Corporate Presentation November 2022.
[15] Sepsis.org. What is Sepsis? Accessed February 2023.
[16] Mayoclinic.org. Sepsis. Accessed February 2023.
[17] Cleveland Clinic. Sepsis. Accessed February 2023.
[18] Penn Medicine. Sepsis. Accessed February 2023.
[19] National Health Service Inform. Sepsis. Accessed February 2023.
[20] Centers for Disease Control and Prevention. What is Sepsis? Accessed February 2023.
[21] Global Sepsis Alliance. Sepsis – A Global Health Crisis. Accessed February 2023.

The prevalence of sepsis is influenced by a variety of factors, including the availability of effective antibiotics, access to healthcare, and the prevalence of chronic illnesses, such as diabetes and heart disease. Improving access to care, increasing public awareness of sepsis and developing effective prevention and treatment strategies can help reduce the burden of sepsis and improve outcomes for those affected.

Causes

Sepsis occurs as a result of an infection, which can be caused by a variety of pathogens, including bacterial, viral, fungal or parasitic infections. Bacteria, such as Escherichia coli (E. coli), Staphylococcus aureus (staph), and Streptococcus pneumoniae (pneumonia), may contribute to the onset of sepsis. Viruses may also aggravate the condition, including human immunodeficiency virus (HIV) and hepatitis C. Fungi, such as Candida albicans, which is commonly found in the gut and on the skin, is another cause. Parasites, such as mosquitos which spread malaria, and Toxoplasma gondii, which can be contracted from undercooked meat, also contribute.

Sepsis can occur when an infection spreads from its original site, such as the skin, lungs, or urinary tract, into the bloodstream. This can trigger an excessive immune response, leading to the release of chemicals that cause inflammation throughout the body and damage to organs and tissues.

Symptoms

The signs and symptoms of sepsis can include fever, chills, rapid heartbeat, rapid breathing, low blood pressure, increased or decreased urination, confusion or disorientation and skin that is warm and clammy to the touch. The severity of sepsis can range from mild to severe, with severe cases requiring immediate medical attention. Other indications of the condition are shortness of breath, nausea or vomiting, diarrhea and abdominal pain. Not all symptoms may be present and they can develop quickly. Sepsis requires immediate medical attention. Early recognition and prompt treatment can improve outcomes and reduce the risk of complications.

Diagnosis

Diagnosing sepsis often requires a combination of laboratory tests, such as blood and urine cultures, and imaging studies, such as X-rays and CT scans. In some cases, a physician may also take a sample of infected tissue for further examination.

Treatment

Treatment for sepsis typically involves a combination of antibiotics to treat the underlying infection and supportive care to address the body's overactive immune response. This may include intravenous fluids, oxygen therapy, and medication to maintain blood pressure and organ function. In severe cases, the sepsis patient may need to be hospitalized and treated in an intensive care unit. A patient's respiratory system may become compromised, and they may require mechanical ventilation to help them breathe. Intubation may also be used if a patient is in septic shock and requires treatment with vasopressors, which are medications that increase blood pressure. In this case, intubation may be necessary to protect the patient's airway during the administration of these medications.

The decision to intubate a patient with sepsis depends on the severity of their condition and the specific needs of the patient. Intubation is a medical procedure that carries risks and can have complications, so it is not used unless critical to the patient's well-being.

Prevention

Preventing sepsis is important and can be done by maintaining good hygiene, getting vaccinated and seeking prompt treatment for infections. Managing chronic conditions, such as diabetes and heart disease, is also important as they increase the risk of developing sepsis.

At Risk Populations

Anyone can develop sepsis, but certain groups are at a higher risk, including infants and older adults which have a weaker immune system and are more susceptible to infections. Other groups include individuals with chronic illnesses such as diabetes, cancer, or lung and heart disease, which can weaken the immune system and increase the risk of infection. Those with weakened immune systems including patients undergoing chemotherapy or those afflicted with HIV/AIDS are also at risk. Hospitalized patients are more likely to be exposed to infectious agents and to develop sepsis as a complication of a medical procedure or hospital-acquired infection. People with severe injuries such as burns, crush injuries, or severe cuts, which increase the risk of infection and people who have undergone recent surgery who may have an increased risk of infection while their immune system recovers.

Sepsis can occur as a result of any type of infection and early recognition and prompt treatment can improve outcomes and reduce the risk of complications.

Approved Treatment and Standard of Care
Treatment of sepsis centers on basic measures such as source control, timely antibiotics, resuscitation, and supportive care for organ dysfunction. Sepsis treatment seeks to control the underlying infection and support the body's vital functions. Several courses of therapy including antibiotics, fluids and electrolytes and oxygen therapy are used to eliminate the underlying pathogen, support blood pressure, prevent organ failure and maintain oxygen levels in the blood. Common broad-spectrum antibiotics used against sepsis include meropenem, piperacillin/tazobactam and vancomycin.[22] A common complication of sepsis is low blood pressure, a condition that calls for vasopressors to restore homeostasis. Steroids may be administered to reduce inflammation and prevent organ damage. In severe cases mechanical ventilation and dialysis are used to support failing organs.

In some cases, other treatments may be required, such as surgery to remove infected tissue or wound care to prevent further spread of the infection. The specific treatment plan for sepsis will depend on the individual case and is adjusted based on the situation.

Early recognition and prompt treatment of sepsis can improve outcomes and reduce the risk of complications. Treatment should be initiated as soon as possible, with ongoing monitoring and assessment to ensure that it remains effective.

Prognosis
The prognosis for someone who has contracted sepsis can vary widely. Some of the factors that impact outcomes include age, overall health, the underlying pathogen, severity of the condition and timing and quality of treatment. Older adults and young children are at higher risk for severe sepsis and complications and individuals with chronic illnesses or weakened immune systems are at higher risk for severe sepsis and complications. Severe sepsis can lead to organ failure and death, while milder cases may resolve with prompt treatment. Most importantly, early recognition and prompt treatment of sepsis can improve outcomes and reduce the risk of complications. Sepsis can still be a serious and life-threatening condition, even with aggressive treatment, and the risk of complications and death remains high for some individuals.

Ongoing monitoring and assessment are essential for individuals with sepsis, and treatment may need to be adjusted as the condition progresses. This accentuates the importance of rapid and accurate biomarker monitoring so patients are able to recover.

Recovery from sepsis can be a slow process, and some individuals may experience long-term effects and complications. The specific outcome for an individual with sepsis will depend on several factors, including the severity of the infection, overall health, age, and timing and quality of treatment. Common long-term effects of sepsis include fatigue, muscle weakness, joint and limb pain, and memory and concentration difficulties. In some cases, individuals may also experience more serious complications, such as organ failure or amputations, which can significantly impact their quality of life.

Economic Impact
Sepsis is the number one cost of hospitalization in the U.S. and the leading cause of death in hospitals. According to the Centers for Disease Control and Prevention (CDC), sepsis is responsible for 1 in 3 hospital deaths and is a leading cause of death for people with a hospital stay of greater than 1 day. It is estimated that each year in the U.S., there are over 1 million cases of sepsis resulting in over 250,000 deaths.

Costs for acute sepsis hospitalization and skilled nursing are estimated to be $62 billion annually. This is only a portion of the total as there are substantial additional costs after discharge for many. The economic impact of sepsis in the United States is significant. According to a study from the Society of Critical Care Medicine, the direct medical cost of sepsis in the U.S. was estimated to be $24 billion in 2013. Additionally, sepsis is the most expensive condition treated in U.S. hospitals, with an average cost per hospital stay of $18,000 to $20,000. Indirect costs such as lost productivity, decreased quality of life, and death also contribute significantly to the overall economic impact of sepsis.

Why is IL-6 the Best Measure?
There are three measures which frequently appear in the literature as important biomarkers for identifying a serious turn in sepsis patients: Interleukin-6 (IL-6), procalcitonin (PCT) and C reactive protein (CRP). When there is trauma due to any number of contributing factors, IL-6 is the first responder in the inflammatory cascade. IL-6 is an early marker of inflammation and is typically produced within hours of the initial inflammatory stimulus. It is produced by a variety of cells in the body, including white blood cells, and acts as a signaling molecule to help activate the im-

[22] Agency for Healthcare Research and Quality. AHRQ Safety Program for Improving Antibiotic Use.

mune response. PCT is also an early marker of inflammation and is typically produced within a few hours of the initial stimulus. It is produced by certain cells in the body, including the thyroid gland, and can be elevated in response to bacterial infections or other inflammatory conditions. CRP is a later marker of inflammation and is typically produced within 48 hours of the initial stimulus. It is produced by the liver in response to signals from IL-6 and other cytokines and can be elevated in a wide range of inflammatory conditions, including infections, autoimmune diseases, and cancer. CRP is a relatively easy biomarker to measure as it appears in much greater volumes than IL-6; however, it may appear too late to take corrective action. New technologies advancing IL-6 measurement, such as the Symphony system may address these limitations.

Chest Pain

Bluejay's secondary tests in development will measure biomarkers related to chest pain, including a high-sensitivity troponin T (hs-TnT) assay and an N-terminal pro-B-type natriuretic peptide (NT-proBNP) assay. These tests can help triage patients with chest pain who may suffer from a variety of conditions. The hs-TnT test specifically identifies proteins that are released into the bloodstream when the heart is damaged, such as in the case of a heart attack or heart injury. In the United States there are more than 800,000 cases of heart attacks annually per the CDC. NT-proBNP is a test that measures the BNP hormone which appears in the blood when the heart is under stress, such as in the case of heart failure, a condition in which the heart cannot pump sufficient blood to meet the body's needs for blood and oxygen. There are about 6.2 million individuals with heart failure per the CDC. The biomarker can provide important data about the severity of the cardiac event and allow providers to appropriately triage and treat the patient.

Chest pain can be caused by a variety of conditions and can have different causes. Some of the common diagnoses related to chest pain are musculoskeletal pain, angina, pulmonary embolism, anxiety or panic attack. There are a number of different causes with differing levels of health impact, making it critical to rapidly and accurately diagnose the problem. The cause can be as severe as a heart attack to as benign as heartburn. Other causes may be:

- Gastroesophageal reflux disease (GERD): caused by stomach acid backing up into the esophagus;
- Pulmonary embolism: caused by a blood clot in the lung, which can be life-threatening;
- Aortic dissection: caused by a tear in the inner layer of the aorta, the large blood vessel that carries blood from the heart to the rest of the body;
- Costochondritis: caused by inflammation in the cartilage that connects the ribs to the breastbone;
- Pleurisy: Chest pain caused by inflammation of the lining that surrounds the lungs.

High-Sensitive Troponin T Assay[23]

A high-sensitive troponin T (hs-TnT) assay is a medical test used to measure the concentration of the protein troponin T in the blood. Troponin T is a specific type of protein that is found in heart muscle cells, and is released into the bloodstream when the heart is damaged or injured. The hs-TnT assay is a highly sensitive blood test that can detect even very low levels of troponin T in the blood, making it a useful tool for early detection of heart damage. This test can be used to diagnose a heart attack, monitor the progression of heart disease, or estimate the risk of future cardiac events.

Compared to traditional troponin T assays, the hs-TnT assay has a much lower threshold for detection, allowing for earlier detection of heart damage. This can help to speed up diagnosis and treatment, and can improve outcomes for individuals with heart disease. It's important to note that while the hs-TnT assay is a useful diagnostic tool, it is not the only test used to evaluate heart health and other tests (such as an electrocardiogram or echocardiogram) may also be required to fully assess cardiac function.

N-terminal pro-B-type Natriuretic Peptide

N-terminal pro-B-type natriuretic peptide (NT-proBNP) is a biomarker used in medical testing to evaluate heart function. BNP (B-type natriuretic peptide) is a hormone produced by the heart that helps regulate blood pressure and fluid balance in the body. NT-proBNP is a fragment of BNP that is released into the bloodstream when the heart is under stress, such as in conditions like heart failure, heart attack, or heart valve problems.

[23] Vaidya, A., *et al*. High-sensitive Troponin T assay for the diagnosis of acute myocardial infarction: an economic evaluation. BMC Cardiovascular Disorders. June 13, 2014.

The NT-proBNP test measures the level of this biomarker in the blood and is used to diagnose and monitor heart conditions, particularly heart failure. Elevated levels of NT-proBNP are indicative of heart failure, and can provide important information about the severity of the condition and the risk of future complications.

The NT-proBNP test is non-invasive, and can be performed with a simple blood draw. Results of the test can be used in conjunction with other diagnostic tests (such as an electrocardiogram or echocardiogram) to evaluate heart function and determine the most appropriate course of treatment for individuals with heart conditions.

Manufacturers of hs-TnT and NT-proBNP tests:

- Roche Diagnostics
  - Elecsys Troponin T-high sensitive
  - Elecsys NT-proBNP
- Abbott Laboratories – Core Laboratories
  - High Sensitivity Troponin Assays
  - Alere NT-proBNP assay
- Siemens Healthineers
  - Cardiac Troponin
  - Stratus CS Acute Care NT-proBNP
- Danaher Corporation (Beckman Coulter)
  - Beckman Coulter Access hsTnI
  - Beckman Coulter Access BNP Assay
- Ortho Clinical Diagnostics
  - Vitros high sensitivity troponin I assay
  - Vitros Immunodiagnostic Products NT-proBNPII Assay

None of these tests are point of care (POC) or near-patient tests and analytes must be transported to dedicated laboratory facilities for analysis. The tests are laboratory-based and require specialized equipment and trained personnel to perform.

Regulatory Pathway

Bluejay has completed several parts of its regulatory checklist for the Symphony analyzer. Initial testing took place in 2021, followed by an FDA pre-submission application in early 2022. Initial clinical trials took place at UT Southwestern and were completed in fall of 2022. Clinical trials will continue in an expansion cohort and a 510(k) filing is expected in 2024. Initially, the primary endpoint was the requirement for invasive mechanical ventilation (IMV). However, as the number of cases of severe respiratory distress for COVID have declined, so has the need for mechanical ventilation. This change has made it difficult to enroll sufficient subjects to complete the study. Bluejay will hold a meeting with the FDA to expand the endpoint to reflect the current standard of care and fully enroll the study. We expect that the endpoint will be 28-day mortality, an endpoint the FDA is familiar with and which was used for the predicate procalcitonin (PCT) test. The design will accept all comers at risk of sepsis and it will explore risk stratification by patient.

510(k) clearance is a pathway used by the U.S. Food and Drug Administration (FDA) to evaluate and approve medical devices. The process name is derived from Section 510(k) of the U.S. Federal Food, Drug, and Cosmetic Act, which requires manufacturers to submit a premarket notification, known as a 510(k) submission, to the FDA before introducing a new medical device to the market.

The purpose of the 510(k) submission is to determine whether a new medical device is "substantially equivalent" to a legally marketed device (referred to as a predicate device) that is already available in the market. The submission demonstrates that the new device has the same intended use and does not raise any new safety or effectiveness concerns compared to the predicate device.

There are multiple steps required. First, the appropriate regulatory pathway must be determined. Then, the sponsor assesses whether their device qualifies for the 510(k) pathway via consultation with the FDA. Some low-risk devices may be exempt from the 510(k) requirements altogether.

The sponsor conducts clinical trials to obtain the necessary data and prepares the 510(k) submission. The package includes information about the device's intended use, technological characteristics, performance data, labeling, and any applicable clinical data. Following the compilation of the package, it is submitted to the FDA along with the required user fees. An FDA review is conducted to assess whether the new device is substantially equivalent to the predicate device where the agency evaluates the scientific, technical and clinical aspects of the submission.

Based on the review, the FDA will issue one of three decisions:

- Clearance: The FDA determines that the new device is substantially equivalent, and a clearance letter is issued. The device can be marketed in the United States.
- Additional information requested: The FDA may request additional data or clarification. The manufacturer must provide the requested information within a specified timeframe.
- Not substantially equivalent (NSE): The FDA determines that the new device is not substantially equivalent to a predicate device. The manufacturer has options to pursue other regulatory pathways or make necessary modifications and resubmit.

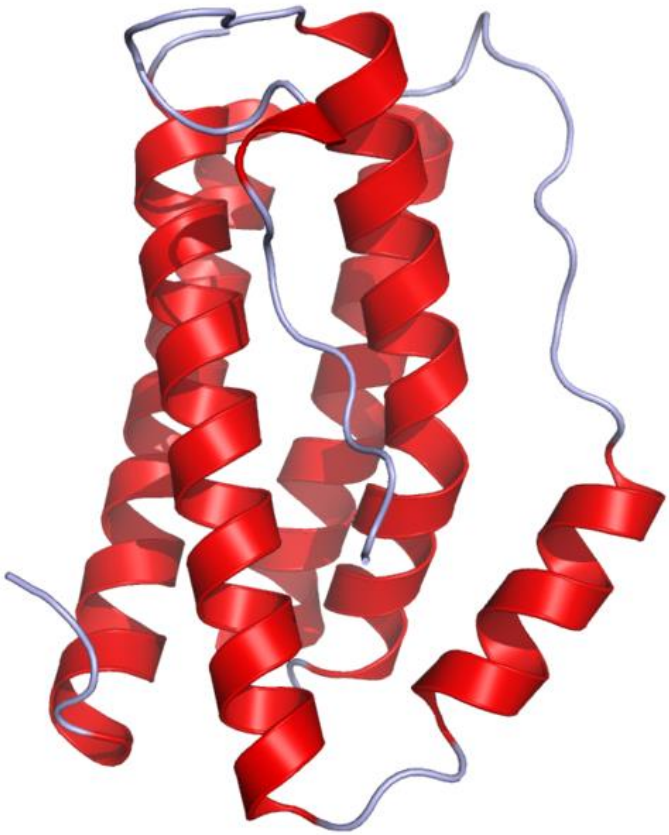
The 510(k) clearance does not involve a comprehensive evaluation of the device's safety and efficacy but rather determines its equivalence to a legally marketed device. The FDA may require post-market surveillance and monitoring to ensure ongoing safety and effectiveness of the cleared device.

Analytes

Interleukin-6 (IL-6)

Interleukin-6 (IL-6) is a pleiotropic pro-inflammatory cytokine produced by multiple cell types including T and B cells, lymphocytes, monocytes and fibroblasts. It regulates immune responses, acute phase reactions, hematopoiesis and bone metabolism. The cytokine is involved in numerous physiological processes such as T cell activation, induction of immunoglobulin secretion, initiation of hepatic acute phase protein synthesis and stimulation of hematopoietic precursor cell proliferation and differentiation. Interleukin-6 is also produced by synovial and endothelial cells leading to local production of IL-6 in joints affected by inflammatory processes such as rheumatoid arthritis. Other associated disorders include Castleman disease, juvenile idiopathic arthritis and Crohn disease. Increases in serum IL-6 are correlated with greater disease activity. IL-6 is rapidly but temporarily produced in response to infections and tissue injuries. Elevated levels are observed in a number of inflammatory processes such as infections, COVID, rheumatoid arthritis, multiple sclerosis, some cancers and neurodegenerative diseases. In these cases, IL-6 can drive excessive inflammation, leading to tissue damage and disease progression.

Exhibit VIII – Crystal Structure of Interleukin 6[24]



Biomarkers

Biomarkers have increased in importance in recent years as detection methods have improved. They provide objective, quantitative measures of biological processes that have advanced scientific understanding and provided insight into understanding underlying biological processes of diseases. Of equal importance is the role of biomarkers to diagnose, monitor and evaluate the effectiveness of treatments.

Many factors have elevated the status of biomarkers including advanced technology such as high-throughput DNA sequencing and proteomics that improve qualification and quantification and a growing understanding of disease biology. A greater focus on precision medicine, which requires the use of biomarkers to identify effective treatments and the need for earlier diagnoses when diseases are more treatable are other driving forces behind the expanding relevance of biomarkers.

[24] Herati, Ramin, rendered using Pymol. Protein Data Bank, Wikimedia Commons.

Sepsis Biomarkers

Sepsis can be difficult to distinguish from other noninfectious conditions in critically ill patients admitted with clinical signs of acute inflammation. Biomarkers can indicate the severity of sepsis and can identify the source of the complication be it bacterial, viral or fungal. A systematic review of sepsis related biomarkers[25] identified 178 candidates that had been used in conjunction with sepsis. Some of the leading biomarkers used include IL-6, C-reactive protein (CRP), procalcitonin (PCT), white blood cell count (WBC) and lactate levels. Measuring IL-6 can serve as an early warning sign of a patient's prognosis and enable quicker and more accurate decision making. Unlike the conventional downstream biomarkers typically used for sepsis, IL-6 is released hours to days before PCT and CRP. However, due to long wait times to receive lab results, IL-6 has had limited utility in time-sensitive triage.

A series of studies[26,27,28,29] have demonstrated IL-6's close tie to mortality above certain thresholds and superior diagnostic and prognostic value. One study in particular noted that IL-6 on day three had a high predictive value for 28-day mortality for sepsis patients.[30] IL-6 is synthesized locally in the initial stage of inflammation or infection and then moves to the liver where acute phase proteins such as CRP are produced. Therefore, elevation of serum IL-6 concentration usually precedes elevation of other inflammatory biomarkers and also clinical signs such as fever making it a leading indicator of response severity. Some studies have even examined the use of multiple markers in combination to enhance the predictive ability; however, one resource notes that using multiple parameters may be clinically and statistically difficult to manage.[31]

IL-6 as a Biomarker

The levels of IL-6 in the blood can be measured through a blood test, called an IL-6 assay. The assay is usually performed as an ELISA (Enzyme-Linked ImmunoSorbent Assay) or a multiplex assay, both of which are simple, sensitive, and specific methods for measuring cytokine levels in a biological sample. These assays use antibodies specific for IL-6 that are conjugated to a detection enzyme, which can be easily quantified to determine the level of IL-6 present in a sample.

Elevated levels of IL-6 can lead to a number of health risks, especially when it comes to sepsis. IL-6 is a contributor in the development of sepsis, as it signals the body to produce an excessive immune response. This leads to a dangerous inflammatory reaction that can damage healthy tissue and organs. High levels of IL-6 are often used as a marker for sepsis and have been linked to a poor prognosis for sepsis patients.

One of the most serious risks of IL-6 and sepsis is the development of multiple organ dysfunction syndrome (MODS). This occurs when the body's immune response causes widespread damage to multiple organs, leading to organ failure. This can include the heart, lungs, liver, and kidneys, among others and can be life-threatening resulting in long-term health problems for patients who survive.

Another risk of IL-6 and sepsis is the development of acute respiratory distress syndrome (ARDS). This is another life-threatening condition that occurs when the lungs become inflamed and filled with fluid, making it difficult to breathe. ARDS is a common complication of sepsis and can lead to respiratory failure and death.

Elevated IL-6 in combination with sepsis can also cause significant cardiovascular problems. This condition has been linked to an increased risk of heart attack, stroke and cardiovascular disease. The immune response triggered by IL-6 can cause inflammation in the blood vessels, leading to the formation of clots which then travel to the heart or brain, causing a heart attack or stroke.

Tests for IL-6 are frequently sent offsite to a reference lab for evaluation, given their low volumes. If the marker is being used to manage critically ill patients, then the 24-48 hours required to return a result is insufficient to guide serious medical decisions.

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[25] Pierrakos, C., Vincent, J.L. Sepsis biomarkers: a review. Critical Care volume 14, Article number: R15 (2010)
[26] Song, J. *et al*. Diagnostic and prognostic value of interleukin-6, pentraxin 3, and procalcitonin levels among sepsis and septic shock patients: a prospective controlled study according to the Sepsis-3 definitions. November 2019, BMC Infectious Diseases volume.
[27] Harbarth, S., *et al*. Diagnostic Value of Procalcitonin, Interleukin-6, and Interleukin-8 in Critically Ill Patients Admitted with Suspected Sepsis. American Journal of Respiratory and Critical Care Medicine. September 2000.
[28] Yu, B. *et al*. Diagnostic and Prognostic Value of Interleukin-6 in Emergency Department Sepsis Patients. Dove Press, September 2022.
[29] Xie, Y., *et al*. 28-day sepsis mortality prediction model from combined serial interleukin-6, lactate, and procalcitonin measurements: a retrospective cohort study. European Journal of Clinical Microbiology & Infectious Diseases. November 2022.
[30] Ryo, Y. *et al*. Accuracy for Mortality Prediction With Additive Biomarkers Including Interleukin-6 in Critically Ill Patients: A Multicenter Prospective Observational Study. Critical Care Explorations. April 2021.
[31] Carcò, D. *et al*. Combination of Interleukin-6, C-Reactive Protein and Procalcitonin Values as Predictive Index of Sepsis in Course of Fever Episode in Adult Haematological Patients: Observational and Statistical Study. Journal of Clinical Medicine. November 2022.

IL-6 Biomarker Advantages

IL-6 offers several advantages compared with other validated biomarkers. Early detection is a key element as IL-6 levels can rise quickly in a patient following the triggering event allowing for the earliest detection and treatment of sepsis or another serious inflammatory episode. This is in contrast to CRP, which is detectable 24 to 48 hours after IL-6. The IL-6 biomarker is a relevant predictor of mortality in sepsis patients, which is an important triage tool to determine the urgency of treatment. IL-6 is a blood-based biomarker, making it relatively easy to obtain and sample. The marker is also tightly correlated with disease severity, further supporting triage efforts. Its utility can help substantially reduce the use of ventilators and better time anti-IL-6 or other ameliorative treatment.

Outside of several COVID-related Emergency Use Authorizations (EUA), no IL-6 test has been cleared by the FDA and they are only used as lab developed tests (LDTs). If granted marketing authorization, Bluejay's Symphony would be the first test fully approved for IL-6 testing.

The FDA has granted Emergency Use Authorization (EUA) for several IL-6 tests during the COVID-19 pandemic. Some of the IL-6 tests that have been granted EUA by the FDA include:

- Elecsys IL-6 test by Roche Diagnostics
- IMMULITE 2000 IL-6 assay by Siemens Healthcare Diagnostics
- Access IL-6 assay by Beckman Coulter, Inc.

Other available but unsanctioned IL-6 Tests:[32]

- RALI-Dx IL-6 Severity Triage Test by SQI Diagnostics
- Immulite IL-6 immunoassay by Diagnostics Products Corporation
- HybriDetect Lateral Flow Assay by Milena Biotec
- VITROS IL-6 test by Ortho Clinical Diagnostics
- IL-6 Test by Randox Laboratories

[32] Lateral flow assays (LFAs) are not sufficiently accurate to guide sepsis triage and are not considered a competitor to the Symphony diagnostic. Sandwich ELISAs are considered to be more precise than LFAs. This is because sandwich ELISAs typically use two antibodies that bind to different epitopes (specific regions) on the antigen. This approach ensures a higher degree of specificity and reduces the risk of false positives or false negatives. In contrast, LFAs typically use only one antibody that binds to a single epitope on the antigen. While LFAs can be accurate and reliable, they are more prone to false positives or false negatives due to the possibility of cross-reactivity with other substances that may be present in the sample. Additionally, sandwich ELISAs generally have a wider dynamic range than LFAs, which means they can detect a wider range of antigen concentrations with greater accuracy.

Intellectual Property (IP)

Toray industries, and, through its license, Bluejay, both rely on two patents that protect the cartridge and the internal design for measuring analytes. US Patent 8,821,813 addresses the design of the cartridge used in the blood analysis and describes its form. It is captioned Liquid-feeding chip and analysis method. The cartridge is composed of several storage tanks connected by channels linked to liquid feeding units that work as a result of rotational inertia and gravity applied to the device.

US Patent 8,409,447, Separation chip and separation method, details the design behind the separation chip for dividing an insoluble component from a suspension using centrifugal force. The device includes a separation liquid holding tank and an insoluble component holding tank arranged in order from an inner circumferential side during rotation, wherein the suspension holding tank and the insoluble component holding tank are connected to each other via a channel. The device is primarily intended to separate blood into an insoluble component and a liquid component.

Bluejay's licensed IP enables a small form factor reader along with the use of cartridges to potentially replace the use of clinical testing laboratories that employ a mass spectrometer. The approach can dramatically increase the speed of generating test results and lower its cost.

Below we list the key patents behind Bluejay's technology:

Exhibit IX – Patents Relied Upon by Bluejay Diagnostics[33]

Title	Patent #	Filed	Expiry	Region	Filer	Link
Separation chip and separation method	8,409,447	27-Jan-09	February '29	US	Toray	x
Liquid-feeding chip and analysis method	8,821,813	20-Nov-08	March '28	US	Toray	x
Separation chip and separation method	Various		February '27	Ex-US	Toray	
Liquid-feeding chip and analysis method	Various		February '27	Ex-US	Toray	

[33] Source: Analyst compiled from public filings and information

Risks

All investments contain an element of risk which reflects the uncertainty of a business and what it will ultimately achieve. Some investments exhibit higher predictability, with current cash flows and established sales. These enterprises will have a lower level of perceived risk while other companies that are developing an undefined, new technology have a much higher level of perceived risk.

The medical device and diagnostic testing space includes companies at both ends of the spectrum, from mega-cap device powerhouses such as Medtronic and Abbott with multiple revenue generating products, to small operations with a handful of employees conducting pre-clinical work. Many of the risks faced by the large medical device companies and smaller single product-focused firms are similar; however, there are some hazards that are particular to smaller companies that have not yet established themselves or their products. The typical risks faced by companies operating in the medical device space include those related to liquidity, financing & trading, clinical trials, manufacturing, partnerships, regulatory, personnel, intellectual property, commercialization and geopolitics.

Liquidity, Financing & Trading

Availability of funding is frequently dependent on the position in the economic cycle. During periods of improving confidence, capital may be easy to obtain; however, during a liquidity crisis or a period of heightened risk perception, even companies with bright prospects may be in trouble if they are dependent on the financial markets to fund their work. Early-stage life sciences firms rely primarily on equity issuance to fund their operations. The duration of early commercialization efforts can be considerable, requiring substantial capital and personnel. Funds can be sourced through debt or equity issuances; however, these sources may reduce the flexibility of the company and can create difficulties if debt is unable to be repaid.

If capital is required to sustain operations and it is not readily available, a company may be forced to suspend commercialization efforts, sell equity at a substantial discount to previous valuations and dilute earlier shareholders. A lack of funding may leave potentially promising products without a viable route forward or force a company to accept onerous terms. In 2020 and 2021, there was a surge of initial public offerings in the life sciences space, and demand for capital increased in sympathy. With multiple demands on cash and tightening capital markets, companies that require a consistent inflow of capital may face difficult terms.

Trading volumes are lower for small life sciences firms, creating liquidity risk for the investor and large transactions may have a material impact on share price. In periods of crisis or heightened risk perception, share price may be volatile. Companies with smaller capitalizations are typically considered riskier and changes in sentiment may adversely affect their trading prices and volumes. Smaller firms may also have less visibility, compete for investor dollars in a shallow market and be excluded from market indices. Share prices may also fall below required thresholds, placing the company at risk of being delisted or forcing it to trade on a less desirable exchange. A low share price may also force a company to effect a reverse stock split, which may be associated with a further decline in price. The result of a declining share price can place investors at severe risk of dilution.

Bluejay Diagnostics has endured operational losses since it has been public and expects to continue to do so into the near future. The company may fail to monetize its development program and may never become profitable. Bluejay has been consistently running clinical trials since it went public in November 2021 where it raised a gross $22 million. As of March 31, 2023 the company holds $6.8 million in cash, which we estimate is sufficient to fund the company's operations until 2H:23.

Clinical Trials

For smaller early-stage companies, investing in new devices is a lengthy process. The timeframe for conducting pre-clinical research to eventually commercializing a new device can take up to a decade or more depending on the regulatory pathway. The FDA provides ongoing guidance as the clinical trial process takes place and may require additional studies before accepting the anticipated 510(k) application for the Symphony device and cartridge.

Bluejay plans to develop several other diagnostic tests, with two in the research stage for diagnosing chest pain. We expect that after the IL-6 test is granted marketing authorization, Bluejay will pursue a similar end for the hsTNT/I and NT-proBNP tests via the 510(k) regulatory pathway. 510(k) is appropriate for products where a predicate device exists.

Manufacturing

Medical product companies can either produce medicines in house or rely on third parties to manufacture them. While there are many benefits to owning manufacturing facilities and exercising direct control, in most cases small and medium size medical device companies work with partners through supply agreements to make their products. Working with a partner confers a number of benefits including economies of scale, a management team dedicated to compliance with regulatory requirements and the flexibility of engaging other manufacturers based on changing circumstances. The use of a partner also limits the capital burden of a single product company and more closely aligns volume, costs and their respective timing. While there are a number of flexibility benefits to outsourcing manufacturing, a sponsor can also be exposed to several risks. Partner manufacturers may not prioritize client projects and may run afoul of regulatory requirements. The manufacturer may experience quality control or volume constraints that could disrupt demand. Take or pay contracts could force the client to accept more product than can be sold in a reasonable time, negatively impacting cash flow and producing excessive inventory which could expire before sale. Bluejay maintains two supplier agreements to manufacture the devices and cartridges. Toray is responsible for the pilot cartridges and Sanyoseiko will serve as the large-scale contract manufacturing organization for test cartridges and Symphony analyzers during full scale production.

Commercialization and Marketing Partnerships

Many smaller pharmaceutical and biotechnology companies lack the financial depth and capital availability to commercialize a product globally. While a US-based company can successfully commercialize in the United States, engaging in this activity on a global basis is more difficult, especially in jurisdictions where regulation, culture and language are substantially different than what is common in the United States. While working with a partner reduces the effort and funds required to commercialize globally and can provide an in-place sales team with active relationships, it reduces the amount of control that the license holder can exercise over the process. Partners may change priorities or fail to invest properly to develop the sublicensed product, resulting in lower sales that expected. Partners may also suffer financial setbacks which prevent them from properly commercializing or meeting milestone obligations. We anticipate that Bluejay will expand outside of the United States after domestic success and will use partners to both obtain approval and commercialize the analyzers and cartridges.

Regulatory

Regulatory risk centers on clinical trial requirements, marketing approval of the candidate, expedited pathways and associated oversight. Regulations extend to post-marketing surveillance and pricing dynamics. Furthermore, device marketing firms typically maintain a global presence and must navigate the regulatory approval process, clinical trial requirements and marketing regulations in the jurisdiction where they seek to commercialize. Substantial expense is undertaken to bring a device through clinical trials and address all of the regulatory agencies' concerns. Companies that have a long history of research success in device development, with opinion leaders and experts advocating for the product in the field will have an advantage. Previous success with the FDA or other regulatory agencies is another attractive attribute for a sponsor. Bluejay's interactions with the FDA will be largely centered on its 510(k) submission that is expected in 2024. We anticipate that additional interaction with the FDA will take place as new tests are developed.

Personnel

Biotechnology startups rely on the expertise and leadership of management to make decisions and investments on their behalf. Competition for talented and experienced management is intense and matching the optimal skill set with the right company is difficult. Change in management can be disruptive if leaders or scientists are lured away by other firms. Additionally, early-stage biotech companies are often virtual and have a small team which can put them at a disadvantage when compared to larger firms, with full-time specialized personnel. A smaller company with much of the financial upside for executives and employees tied to stock price may deter certain talent from joining the firm. Bluejay appointed a new Chief Financial Officer, Kenneth Fisher, in March 2022 following the resignation of previous CFO Gordon Kinder who left to pursue other interests.

Intellectual Property

Despite the existence of patents and trade secrets, infringement of intellectual property is a risk. Bluejay's intellectual property protection is licensed from Toray Industries, which is responsible for maintaining the licenses and ensuring that there are no patent violations. Toray's agreement with Bluejay has many stipulations regarding required license payments and development milestones. If Bluejay is unable to meet these requirements, it may put the license agreement in jeopardy. While the protective patents can prevent others from using the same technology as used in the Symphony system, technology can be circumvented and approaches can be copied if they demonstrate success, raising the risk that the platform could be imitated or replicated, especially by a larger firm with more resources. The underlying technology used in the test, ELISA, has been used since the 1970s and its basic technology is no longer subject to patent protection. Bluejay's intellectual property rights largely protect the design behind the simplicity of use and rapidity of the test cartridges which could be threatened if the product becomes commonplace.

Market Risk

Successful marketing of cleared medical devices relies on adoption by patients and providers. An approved diagnostic test must have convincing clinical trial data and maintain a favorable reputation among users. Marketing is expensive and requires an experienced sales force and a presence in the marketing area. Marketed products remain under surveillance and any unexpected adverse effects may lead to regulatory authorities revoking marketing authorization. Inclusion of the diagnostic test in standard emergency facility protocols for triage would be an important element of Symphony's success. Rapidly penetrating emergency room, long-term acute care facility and intensive care units and familiarizing providers with the benefits of the test are key to success. Profit margin for all parties is another important element. It must be sufficient to provide incentive for the facility to run the test in the existing reimbursement environment. The utility of the offering must also address an unmet need better than other options. We expect that Bluejay will use a hybrid model of commercialization in the United States, using its own sales force and leveraging the reach of distributors. If further distribution is sought outside of the United States, commercialization and marketing will likely be performed by partners.

Geopolitical

Recent trade tensions between the US and China threaten the world economy, and have been exacerbated by the recent pandemic. There had been a cross-pollination of capital and drug development between China and the United States which has slowed as a result of the trade and political dispute between the countries. This conflict may reduce the availability of capital, partnerships and future development and commercialization deals between companies in the two nations. The UK withdrew from the European Union on January 31, 2020 creating additional trade, transportation and other barriers between the UK and mainland Europe. Conflict between Ukraine and Russia has led to disruptions in clinical trials in these countries. Sanctions have also been placed on Russia and many of its businesses which may lead to product shortages. Refugees fleeing the war in Ukraine may also impact nearby countries and their productivity which could affect clinical trials and commercialization in these areas.

Peers & Competitors

Many participants contribute to the testing space, including in vitro diagnostic (IVD) tests, point-of-care (POC) tests, imaging tests and molecular diagnostics among others. Within each of these categories, there are a number of different companies and organizations that compete for market share.

POC testing refers to diagnostic tests that can be performed at the bedside or in other settings outside of the traditional laboratory. It includes a wide range of tests such as blood glucose monitoring, pregnancy testing and infectious disease testing. This category includes Bluejay's Symphony system.

One of the key drivers of the POC testing market is the increasing demand for faster and more convenient methods, particularly in settings such as emergency departments, ambulances, rural hospitals and primary care clinics. This has led to the development of new POC testing technologies that are faster, more accurate and easier to use than traditional laboratory-based testing. In terms of market structure, the POC testing market is highly fragmented, with many competitors. This includes large multinational companies such as Abbott, Roche, and Siemens, as well as smaller niche players such as Alere, Quidel and Trinity Biotech.

In addition to established players, there are also a number of start-ups and emerging companies that are entering the POC testing market with new technologies and business models. These companies may be focused on developing innovative new tests or platforms, or may be targeting specific niches or patient populations.

The focus of Bluejay's lead program is sepsis triage. There are a number of approaches to detect sepsis, ranging from blood and imaging tests to assessment scores, microbiological cultures and biomarkers. Several tests for IL-6 pursued emergency use authorization (EUA) and were discussed in a previous section. Devices are used to run many of these tests including blood culture systems, lactate meters and pulse oximeters among others.

The leading players in the diagnostic testing space include Abbott Labs which offers a broad variety of POC tests with its Afinion multi-system analyzer. Siemens offers its Immulite and ADVIA Centaur immunoassay systems which provide access to hundreds of assays. Another dominant player is Roche and its cobas modular analyzer in the blood borne disease, respiratory, oncology, sexual health and transplant testing markets. Hologic markets its Panther Fusion module and Aptima assays in virology, sexual health, infectious disease and other areas. Quidel offers a selection of diagnostics from rapid immunoassays to confirmatory nucleic acid testing from a number of brands including MicroVue, Sofia and Triage. Ireland-based Trinity Biotech operates in the POC segment providing diagnostic products for infectious disease with ELISA, antibody, Western blot and other tests offered. Beckman Coulter sells lab workflow automation equipment which provides test services in chemistry, hematology and immunoassay. Other test manufacturers and distributors include Milenia Biotec with a competency in lateral flow POC tests, Ortho Clinical Diagnostics, which sells IL-6 reagent packs, SQI Diagnostics which is developing an IL-6 test, Bio-Rad Labs and Cepheid.

IL-6 tests are offered in many formats from lateral flow assays[34] which lack the precision required to properly diagnose sepsis to central-lab based machines running immunoassays.

[34] Rahbar, M., *et al*. Sensitive Colorimetric Detection of Interleukin-6 via Lateral Flow Assay Incorporated Silver Amplification Method. Frontiers in Bioengineering and Biotechnology. November 2021.

Exhibit X – Diagnostic Testing Public and Private Companies[35]

Ticker	Company	Price	MktCap (MM)	EV (MM)	Therapeutic Area
RHHBY	Roche	$39.85	$272,176	$273,750	cobas e analyzers
DHR	Beckman Coulter	$227.18	$167,636	$180,186	Access 2 PCT IL-6, DxA 5000, UniCel DxI
ABT	Abbot Labs	$101.71	$176,868	$181,951	Molecular POC test, ID Now , Afinion 2
SIE.DE	Siemens	€ 156.66	€ 125,020	€ 156,160	Immulite system, ADVIA Centaur
HOLX	Hologic	$78.66	$19,360	$19,592	Diagnostic products: Aptima
BIO	Bio-Rad Labs	$379.76	$11,244	$10,585	Bio-Plex Multiplex Immunoassay System
QDEL	Quidel	$86.49	$5,763	$7,746	Molecular diagnostics, immunoassays
TRIB	Trinity Biotech	$0.90	$34	$98	POC diagnostics: infectious disease/Immunoassays
SQIDF	SQI Diagnostics	$0.05	$21	$26	Rali-Dx IL-6 test in development
private	Milenia Biotec				Lateral flow POC tests, immunoassay
private	Ortho Clinical Diag				IL-6 reagent packs & Vitros system
private	Cepheid				Molecular systems/tests: organisms & genetic diseases
BJDX	Bluejay Diagnostics	$0.19	$4	($3)	Symphony IL-6 POC ELISA test

[35] Price as of May 30, 2023

Management Profiles

Neil Dey, Ph.D. President, Chief Executive Officer and Director

Dr. Dey co-founded Bluejay Diagnostics in 2015, after co-founding Lana Management & Business Research International (LMBRI) in 2007. The LMBRI management consulting company is focused on the launch and marketing of medical products in the US, Japan and EU.

Dr. Dey spent approximately eight years at LMBRI, consulting with companies such as Toray Industries, Hitachi Chemicals (now Showa Denko Materials) and Fuji Chemicals. Prior to this, he held executive positions at several firms. From 2005–07, he was Vice President of Business Development and Market for Definines, AG (acquired by AstraZeneca). From 2001–05, he was Head of Business Development, Western US, at IMPATH, Inc. where he handled three business units and the introduction of a new product, Her2neu Diagnostics, for the treatment of breast cancer, with Herceptin. Dr. Dey was also Chief Business Officer at Genmethrax, Inc; Manager, Technology Licensing, Thomas Jefferson Medical University; and Manager, Technology Licensing, Ciba Geigy (Novartis).

Dr. Dey earned a Bachelor of Science and Master degree in Biochemistry from Visva-Bharati University in India and Ph.D. in Lipid Membrane Biochemistry from Biological Research Center in Hungary. He also holds a Master of Business Administration degree (Fulbright Scholarship) from the University of Cambridge.

Kenneth Fisher, Chief Financial Officer

Mr. Fisher joined Bluejay in 2022. Prior to this, from 2010 to 2021, he was Executive Vice President, Chief Financial Officer and Treasurer of Meridian Bancorp, Inc., a $6.6 billion NASDAQ-listed financial institution, and its subsidiary, East Boston Savings Bank (merged with Rockland Trust in November 2021). Prior to that, he served as Vice President and Treasurer at Beverly National Bank and as a senior auditor at Parent, McLaughlin & Nangle, CPAs (now Marcum LLP).

Mr. Fisher is a Certified Public Accountant. He received his Bachelor Degree in Business Administration from the Isenberg School of Management at the University of Massachusetts at Amherst and is a graduate of the New England School for Financial Studies.

Jason Cook, Ph.D. Chief Technology Officer

Dr. Cook joined Bluejay in 2021. From 2014–21, he served as Chief Executive Officer at NanoHybrids, Inc., a nanotechnology company focused on developing theranostic nanoparticle platform technologies. Here, he was Director and Chairman of the Board from 2020–21 and Senior Scientist from 2014–17, overseeing the development of several core technologies.

Dr. Cook did his PhD in Biomedical Engineering from The University of Texas at Austin, focusing on the design and development of medical diagnostic systems. His postdoctoral work included improving the bioconjugation strategies of nanoparticles for molecular targeting. Dr. Cook also serves as *ad-hoc* reviewer for numerous panels at the National Institute of Health and peer-reviewed scientific journals.

Operational Milestones

Bluejay Diagnostics has been working on its mobile diagnostic testing initiative for over a decade. The effort is underlined by the company's collaboration agreement with Toray Industries to develop a point of care (POC) or near patient test for IL-6 patients. Initial work for Bluejay focused on an allergic conjunctivitis test (Allereye) which was eventually cleared by the FDA and granted the CE mark in Europe in 2019. In December 2020, an agreement was signed with Toray to advance an IL-6 test to identify and triage patients at risk for mechanical ventilation. During this time, Bluejay had been operating as a private company; however, with the improvement in public market sentiment for small cap device companies and the need for capital to advance the IL-6 program, an initial public offering was planned and later executed in November 2021. $21.6 million in gross proceeds were raised and the company began trading on the NASDAQ under the ticker BJDX on November 10, 2021.

Following the IPO, efforts began in earnest to evaluate the Symphony device in COVID patients, given the strong correlation between high levels of IL-6 and mortality. A 90-patient multicenter clinical study was conducted in critical care patients in Texas, with data available in January 2022. Shortly thereafter, Bluejay announced a pre-submission filing with the FDA for the Symphony IL-6 test. In March 2022, according to a planned transition, Kenneth Fisher assumed the role of Chief Financial Officer. In the regulatory sphere, the FDA provided feedback suggesting the recommended route for submission of the IL-6 diagnostic. While initially Bluejay expected that a submission might be possible by year end 2022, completing its planned studies by July 2022, this was extended by several quarters as the precise endpoints desired by the FDA had not been clarified and an extension was required.

As discussions with the FDA progressed in the first months of 2023, Bluejay emphasized building a network of advocates and key opinion leaders (KOLs) that recognize the value of the Symphony IL-6 diagnostic. Data from the study completed last July was published, demonstrating a 98% negative predictive value to identify COVID patients at risk for severe illness. Following the turn of the year, Bluejay signed a collaboration agreement with the Blood Centers of America (BCA) which will develop relationships that can lead to the ultimate use of the Symphony system in the blood and hospital markets. The relationship is expected to provide awareness and access to BCA members.

In May 2023, Bluejay provided an update on its regulatory strategy and plans to request a pre-submission meeting with the FDA to clarify the intended endpoint for its IL-6 test for risk stratification of hospitalized sepsis patients. The anticipated timeline calls for continued trials that are expected to enroll quickly given the larger population of patients. Management anticipates that the study will be complete in 1H:24 to be immediately followed by a 510(k) submission. A response should be provided within three months; however, additional time may be required for the sponsor to respond to FDA information requests. This suggests that a response could be available before year end 2024,

Key milestones:

- Collaboration agreement with Toray Industries for IL-6 test - 2020
- Initial Public Offering – November 2021
- Completion of 90 subject COVID triage study – January 2022
- Filing of pre-submission package – January 2022
- Kenneth Fisher appointed as Chief Financial Officer - March 2022
- FDA recommends pathway to grant Symphony IL-6 test marketing authorization - June 2022
- Multiple Symphony IL-6 clinical study milestones achieved – July 2022
- KOL event: IL-6 as Critical Care Biomarker – August 2022
- Collaboration agreement with Blood Centers of America – February 2023
- Regulatory strategy refinement – May 2023
- FDA pre-submission application – 2Q:23
- Completion of pivotal trial for IL-6 – 1H:24
- Submission of 510(k) application – 1H:24
- FDA response to 510(k) submission – 2H:24

On May 10th, 2023, Bluejay reported 1Q:23 financial and operational results and filed Form 10-Q with the SEC. For the quarter ending March 31, 2023, no revenues were reported, as to be expected by a development stage company. Operating expense was ($2.7) million yielding a net loss of ($2.5) million or ($0.12) per share.

For the three months ending March 31, 2023 and versus the same period ending March 31, 2022:

- Research & development expense totaled $1.4 million, rising 95% from $0.7 million, driven by the addition of new personnel, clinical program expansion to support the anticipated FDA submission;
- General and Administrative expenses were $1.2 million vs. $1.3 million on an increase in scalable infrastructure investment, as well as expenses to support public company operations due to the completion of the initial public offering;
- Sales and Marketing expense was $148,000, up 176% from $54,000. Funds were allocated to efforts to improve awareness of the Symphony system with KOLs and other advocates;
- Net loss was ($2.5) million vs. ($2.0) million or ($0.12) and ($0.10) per share, respectively.

As of March 31, 2023, cash and equivalents stood at $6.8 million. This amount compares to a $10.1 million balance in cash and equivalents held at the end of 2022. Cash burn for 1Q:23 was ($3.3) million with a small draw on financing cash flows related to withholding tax on grant of issued stock.

Valuation

Bluejay Diagnostics is an early-stage diagnostic device company with a lead program for triage in sepsis using the IL-6 biomarker and its Symphony diagnostic platform. Despite the availability of IL-6 testing, low volumes for the IL-6 analyte require that the tests be shipped elsewhere for analysis, frequently requiring 24 to 48 hours to provide results. Even if there is an onsite lab that has sufficient volume to justify running the IL-6 test[36], the blood must still be centrifuged before analysis and transported to the central lab to wait in queue for sufficient volume to justify a run. The need for point of care diagnostics is even more pronounced in rural settings, at remote military facilities and other areas that are outside geographies adjacent to major medical centers.

While IL-6 is Bluejay's first pursuit, there is substantial opportunity for other tests which are relatively low volume or need to be run in remote areas too small to justify a reference lab. Bluejay is considering the next series of tests to address chest pain; however, the opportunities are boundless and there is substantial unmet need where quick turnaround is needed in low volume conditions.

Our valuation model evaluates IL-6 for sepsis triage and will add other indications as they are developed or become more apparent. We examine development of the Symphony system in the United States where there are about 1.7 million adults that are diagnosed with sepsis. According to the CDC, there are also 131 million emergency room visits every year for any cause and over 5,000 emergency rooms in the country. This helps define and place in context the addressable market of 1.7 million.

Bluejay is in process of completing its pivotal trial for the IL-6 diagnostic in sepsis triage. We anticipate that the study will wrap up before year end and data will be available in early 2024. This will be followed by a submission of a 510(k) package to the FDA in mid-2024 and we expect a grant of marketing authorization in 2025. Concurrent with the FDA review process we expect that Bluejay's management team will be working on commercialization activities to advance sales and marketing efforts both internally as well as with partners and distributors. We assume that first sales of the Symphony cartridges begin in 2025.

Our model is driven by penetration into the addressable market of 1.7 million diagnosed cases of sepsis every year. We forecast this number to grow by 0.4%, along with population increases and estimate that in year one there will be 60 basis points of penetration into this market. By year two, this will increase to 1.3% and then consistently rise to 36% by 2034. We assume that the immuno-analyzer will be sold at cost and profits will be driven by the sale of cartridges. Tests are expected to sell for $150 per cartridge with 2023 representing the base year for price and inflation adding 3% per annum thereafter. These assumptions generate steadily increasing revenues that rise to $133 million by 2034, the year of peak penetration.

Our assumptions assume a 50% gross margin in the first year of sales, rising to 75% gross margin by the sixth year. Bluejay will have a third-party manufacturer assemble the readers and cartridges and will allow some margin to incentivize distributors. Low volume in the early years will pressure margins due to fixed costs; however, we see these spread over sufficient units after several years to reach the terminal gross margin rate in 2029.

We anticipate research and development costs to range from $2.2 to $2.5 million over the period captured by our discounted cash flow model that pertains to the IL-6 test. Following the required work for the IL-6 test, we anticipate development of further tests and cartridges for chest pain (hsTNT/I & NT-proBNP) and other low volume diagnostics that require quick turnaround.

General and administrative costs are running in the $5 million per year range and we expect a low single digit inflation rate in this line item over the course of our forecasts. Sales and marketing expense will slowly ramp up over the next year and a half as a team of eight is assembled rising to $1.5 million in 2024 and $1.8 million in 2025. Research and development expenses are expected to fall in 2023 as the majority of trial costs have been incurred. The amount is expected to fall again in 2024 as the 510(k) application is submitted. Work on other diagnostic tests is expected to accelerate in the following years. Cash taxes are forecast at 25% and will be assessed after the use of net operating losses (NOLs).

Probability of success (PoS) is an important component of our valuation model and a number of factors drive its value. Some of the elements considered include the appropriate regulatory pathway, strength of the data generated in clinical studies and the ability of manufacturing and other partners to satisfy current good manufacturing practices

[36] Based on our review, the large analyzers such as those sold by Roche, Siemens and Beckman Coulter require somewhere around 100 tests to justify the setup for a specific analyte run.

(cGMP) among other elements. We apply a 50% likelihood of ultimate commercialization and recognize the disclosure of data from the ongoing study and acceptance of the 510(k) application as other milestones where the probability is reassessed.

We use a discounted cash flow (DCF) model to value Bluejay's cash flows employing a 15% discount rate. We assume outstanding warrants below our target price will be exercised, and add resulting cash to the balance sheet. Capital raises will be required in the near future to support ongoing clinical trials and initial commercialization. We estimate that additional shares will be issued in 2023 at recent market prices to raise $10.0 million to support company operations.

The result of our forecasts and estimates generates a valuation and present value of Bluejay Diagnostics of $2.00 per share.

Conclusion

Bluejay Diagnostics has identified a niche in the diagnostic testing market that calls for low-volume, high accuracy tests for critical diseases. While the first foray into point of care testing is in sepsis, there are many other opportunities for rapid turnaround tests and a severe unmet need for diagnostic results to inform medical decision making.

Sepsis is a leading cause of death in hospitals and physicians require accurate data on patient status before treatment. Existing testing approaches frequently require several time-consuming steps before a diagnostic can be run, consuming valuable time. Transportation, preparing the sample and waiting in queue for sufficient volume to justify a test require 24 – 48 hours to produce a result when physicians need answers immediately. Due to the lack of timely testing, we think Symphony could drive a substantial increase in volume in IL-6 test demand, especially at the price point anticipated, to help guide physician decision making in the emergent care.

Bluejay's Symphony diagnostic is able to accept a small whole blood sample in the available cartridges and run the test in the analyzer with up to six cartridges to produce a result in less than 20 minutes. The diagnostic cartridge and machine are inexpensive enough to justify at any emergent care facility and even in the field for remote operations or military hospitals as the immuno-analyzer has its own power supply. If Bluejay is successful and can in the future offer many diagnostics that can be rapidly deployed anywhere, the device becomes even more valuable and could carve out an important niche in diagnostic testing where an accurate results and rapid results are critical to patient care. Other indications in the pipeline to be pursued after the sepsis triage test is granted marketing clearance include chest pain diagnostics hs-TnT and NT-proBNP.

Clinical trials are now underway in the United States and Bluejay is in contact with the FDA to decide the proper primary endpoint and regulatory pathway for its ongoing study. The initial endpoint was the use of mechanical assisted ventilation; however, since there are now fewer incidents of severe respiratory distress, the company has settled on the use of 28-day mortality and risk stratification of hospitalized sepsis patients. Our estimates call for the trial to be completed in 2024, followed shortly after by a regulatory submission using the 510(k) pathway. We further anticipate that a grant of marketing authorization will emerge before year end 2024, followed by commercialization. Bluejay has identified its market and plans to engage a small team of sales and marketing personnel in combination with partners and distributors sell the devices and cartridges.

While we see a modest level of risk as Bluejay works out the details of the clinical trial and raises additional capital, we also see substantial opportunity in a market that lacks the type of testing necessary to make important medical decisions, especially in low volume, time sensitive situations where accuracy is paramount.

Key reasons to own Bluejay Diagnostics shares:

- **Symphony system offers several advantages over traditional systems**
  - **Ease of use**
  - **Cost, time and space savings**
  - **Versatile platform able to support a broad test menu**
  - **Throughput and multiple testing capability**
  - **Immediate test of analyte, which can degrade during wait in queue**
- **Bluejay holds global license (ex-Japan) for manufacturing, marketing and sale of Symphony system**
  - **Domestic commercialization using small sales force and distributors**
  - **Ex-US commercialization using partners and distributors**
- **Further expansion into additional low volume, quick turnaround tests**
  - **Chest pain markers**
  - **Autoimmune disease**
  - **Inflammatory diseases**

Based on our analysis of Bluejay's diagnostic, its lead program and follow on indications, we initiate on the company with a valuation of $2.00 per share.

PROJECTED FINANCIALS

Bluejay Diagnostics, Inc. - Income Statement

Bluejay Diagnostics, Inc.	2022 A	Q1 A	Q2 E	Q3 E	Q4 E	2023 E	2024 E	2025 E
Total Revenues ($US '000)	**$249**	**$0**	**$0**	**$0**	**$0**	**$0**	**$0**	**$1,636**
YOY Growth								
Cost of Goods Sold	$200	$0	$0	$0	$0	$0	$0	$736
Product Gross Margin	20%	0%	0%	0%	0%	0%	0%	55%
Research & Development	$4,152	$1,355	$800	$600	$500	$3,255	$2,000	$2,200
General & Administrative	$4,763	$1,177	$1,290	$1,125	$1,265	$4,857	$4,900	$5,350
Sales & Marketing	$451	$148	$115	$121	$114	$498	$500	$1,800
Income from operations	($9,318)	($2,680)	($2,205)	($1,846)	($1,879)	($8,610)	($7,400)	($8,450)
Operating Margin								
Other Expense	$21	$140	$0	$0	$0	$140	$0	$0
Pre-Tax Income	($9,297)	($2,540)	($2,205)	($1,846)	($1,879)	($8,470)	($7,400)	($8,450)
Provision for Income Tax	$0	$0	$0	$0	$0	$0	$0	$0
Tax Rate								
Net Income	**($9,297)**	**($2,540)**	**($2,205)**	**($1,846)**	**($1,879)**	**($8,470)**	**($7,400)**	**($8,450)**
Net Margin								
Reported EPS	**($0.46)**	**($0.12)**	**($0.07)**	**($0.04)**	**($0.04)**	**($0.24)**	**($0.17)**	**($0.16)**
YOY Growth								
Basic Shares Outstanding	20,164	20,375	32,475	44,050	44,110	35,253	44,215	51,540

Source: Company Filing // Zacks Investment Research, Inc. Estimates

HISTORICAL STOCK PRICE

Bluejay Diagnostics, Inc. – Share Price Chart[37]

[37] Source: Zacks Research System

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