

# Ascendant Dx

## Business Plan





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## Ascendant Diagnostics

### Company Overview

Ascendant Dx is an early stage bioscience company whose mission is to commercialize disruptive diagnostic technologies aiding identification and treatment for diseases of women and children. Our particular focus is on cancer, autoimmune diseases and serious childhood afflictions.

Ascendant's first product (Melody™) is a simple and highly effective diagnostic to detect early stage breast cancer by detecting specific proteins present in tears. First sales and CE Mark are anticipated in 2017. Follow-on Melody programs will monitor treatment prognosis and examine recurrence of breast and other cancers.

### Company History

Ascendant was founded in 2011 as a portfolio company of VIC Technology Ventures. Ascendant has three pending patent applications and will be submitting two more applications by the end of 2015. Funding to date has been \$2.5M in grants and equity investments.

### Market Need

Ascendant's Melody is targeting all women in the population – empowering them to take personal control of their breast health. Mammograms have >80% sensitivity in women with fatty breasts, however >40% of women have breasts consisting of dense tissue and mammogram sensitivity is reduced to <25% for these women. We initially target Melody to be a yearly, simple point-of-care diagnostic for women in both the developed and developing markets.

### The Problem

The current gold standard in breast cancer screening is mammography, which has the following disadvantages:

- Ineffective at detecting tumors smaller than 2cm
- Ineffective in women with dense breast tissue
- Painful: pressure equivalent to 40 lb car battery
- High false positive rate and low sensitivity
- Expensive
- Inaccessible to patients in low income and rural areas

### The Solution

Our tear-based test will provide the following advantages:

- Not limited by tumor size for identification
- Not limited by tissue type
- Pain free
- Highly sensitive and specific
- Low cost
- A point-of-care device for a physician's office
- Results can be monitored within 30 minutes

### Key Team Members

Ascendant has a talented management team with more than 50 years experience in technology development, new venture creation, financing, market research and biophysical characterization of proteins.

**Omid Moghadam** - CEO

**Patricia Beckmann, Ph.D.**-  
CSO and CBO

**Suzanne Klimberg, M.D.**-  
CMO

**Debby Winters, Ph.D., J.D.**-  
Legal Counsel

**Anna Daily, Ph.D.**- Chief  
Scientist

**Lindsay Rutherford, Ph.D.**-  
Senior Scientist

Ascendant has strategic partnerships (such as Peace Health in Portland, Oregon) and outsources specific tasks to (clinical, regulatory, bio-statistical, accounting, etc.).

Our Scientific Advisory Board and Members of Board of Directors are all successful clinicians, have commercialized technologies, financed and/or built successful companies.

### Contact Information

**Name:** Omid Moghadam

**Title:** CEO

**Email:** omid@asndx.com

### Company Address:

1200 Stewart Place  
Springdale AR 72764  
Phone: 479.973.3911



### ◆ COMPANY HISTORY

#### History

Ascendant Dx was incorporated as a limited liability corporation in 2011 and is headquartered in Springdale, Arkansas. Ascendant Dx was founded by Omid Moghadam as one of a portfolio of companies founded at VIC Technology Ventures, a venture creation firm specializing in commercializing early-stage university based inventions. For the past four years, the Ascendant team has been working to develop Melody™, a diagnostics assay for breast cancer screening of women with dense breasts.

#### Capitalization

Ascendant Dx has raised a seed round of \$450K and a Series A round of \$1.75M. The investors include a strategic investor (Hospital and lab company), and a number of professionally managed angel funds in addition to a number of high net worth individuals. Ascendant also currently has a non-dilutive Small Business Innovative Research grant (SBIR) totaling \$175K. Other non-dilutive grants are currently being submitted. In addition, Ascendant is currently raising \$5M to fund the Melody™ clinical trials and regulatory clearances for:

- 1) Early diagnosis of breast cancer,
- 2) Monitoring prognosis during treatment and
- 3) Follow-up for recurrence in patients who have been treated and are cancer free.

Financial projections for the company are found in Appendix I.

#### Team

Ascendant Dx today employs five corporate employees and 8 part-time contractors in accounting, business development, clinical research, public relations and strategy roles and is advised by an experienced and high profile advisory team. Full biographies for the Team, Scientific Advisory Board and Board of Directors are found in Appendix II.

Ascendant's team consist of:

Omid Moghadam – CEO and Chairman: Mr. Moghadam has 23 years of invention and commercializing of new technologies at companies such as Intel and Kodak. He has founded and managed numerous start-up companies.

Dr. Patricia Beckmann – CSO and CBO: Dr. Beckmann has 30 years of experience in research, management, law and finance in biotechnology and diagnostics companies. She spent the majority of her career at Immunex and Amgen and was founding CSO of Homestead Clinical (now Integrated Diagnostics).

Dr. Suzanne Klimberg – CMO: Dr. Klimberg discovered breast cancer protein patterns in tears and is a co-inventor of the company's first product, Melody™. In addition to her duties at Ascendant, she is a practicing breast surgeon at University of Arkansas Medical School.



Dr. Debby Winters - Legal Counsel: Dr. Winters, the principal of the Winters Law Firm focuses on corporate and intellectual property law. She has a Ph.D. in Biochemistry and Molecular Biology and graduated magna cum laude from the University of Arkansas Law School, where she was on the Arkansas Law Review.

Dr. Anna Daily – Chief Scientist – Melody™: Dr. Daily is the chief scientist on the Melody™ project. Her efforts since the founding of the company have been focused on discovering biomarkers for incorporation in the Melody™ assay.

Dr. Lindsay Rutherford – Senior Scientist, Platforms: Dr. Rutherford leads Ascendant's efforts in platform development for Melody™ and other projects.

### Board of Directors

The Board of Directors has breadth with subject matter and entrepreneurial business expertise. Their Biographies are found in Appendix II.

Mr. Omid Moghadam – CEO and Chairman

Dr. Steve Harms – Non Executive Director: Dr. Steven Harms is an internationally recognized clinical radiologist and breast cancer specialist, entrepreneur and inventor.

Dr. Amit Mehta - Non Executive Director: Dr. Amit Mehta is the Vice-President and co-founder of Intrinsic Imaging, LLC, an imaging contract research organization that specializes in utilizing imaging biomarkers for clinical trials.

Dr. Brigitte Piniewski - Non Executive Director: Dr. Piniewski is the Chief Medical Officer of Peace Health Laboratories, which services Alaska, Washington and Oregon.

Mr. Richard Bond - Non Executive Director: Mr. Dick Bond has over forty years of business experience in the food industry and previously was President and Chief Executive Officer of Tyson Foods.

### Scientific Advisory Board

The Scientific Advisory Board includes several distinguished scientists:

Dr. Suzanne Klimberg (CMO and Chair of the SAB).

Dr. Patricia Beckmann (CSO and CBO).

Dr. Isaac Kohane MD, PhD: Co-Director of the Center for Biomedical Informatics at Harvard Medical School.



Dr. Mark Boguski MD, PhD: Faculty of Harvard Medical School and Beth Israel Deaconess Medical Center in Boston where he founded the Genomic Medicine

Mr. David Green: MacArthur Fellow, Ashoka Fellow and is recognized by the Schwab Foundation as a leading social entrepreneur. A serial entrepreneur, David develops ventures that use medical and health technology to make healthcare easier and more affordable.

### Strategic Partners

Peace Health Inc. ([www.peacehealth.org](http://www.peacehealth.org))

Peace Health is an integrated delivery network of hospitals, clinics and laboratories with installations in Alaska, Oregon and Washington states in the US. Peace Health Is a strategic investor in Ascendant Dx and Peace Health Laboratory's Chief Medical Officer, Dr. Brigitte Pinewski, is a member of Ascendant's board of directors. In addition, two of Peace Health clinics are also participants in Ascendant Dx validation trials.

Peace Health Laboratories ([www.peacehealthlabs.org](http://www.peacehealthlabs.org))

Peace Health Labs, a subsidiary of Peace Health is a laboratory and sales partner of Ascendant's. Peace Health Labs is a comprehensive lab chain with new test development capability and a national sales team.

### Validation Partners

University of Arkansas ([www.uark.edu](http://www.uark.edu))

Ascendant Dx has worked with both the Mass Spectrometer center and the Department of Biomedical Engineering on discovery and assay development projects.

University of Arkansas for Medical Sciences ([www.UAMS.edu](http://www.UAMS.edu))

Ascendant Dx is working with the Proteomics Core Lab at UAMS on analysis of samples in the discovery and validation stages of assay development.

### Development Partners

Now Dx Inc. (<http://www.nowdx.com>)

Now Dx is a diagnostics company is developing a simple, inexpensive point of care suite of diagnostic tests based on a platform developed at ZYX Corp of Toronto, Canada. Now Dx recently acquired ZYX Corp. Ascendant Dx is working with Now Dx to develop a simple point of care test for Melody™.

### Clinical Partners

In the course of validation and early clinical trials of Melody™, Ascendant Dx has signed agreements with a number of breast cancer clinics. These include:

- The Breast Center, Fayetteville, Arkansas
- Breast Surgery of Tulsa, Oklahoma
- Knoxville Comprehensive Breast Center, Knoxville, Tennessee
- Peace Health Southwest, Portland, Oregon



- Peace Health Longview Surgery Center Long View, Washington
- Highland Oncology Clinics, Springdale, Arkansas

### ◆ PRODUCTS

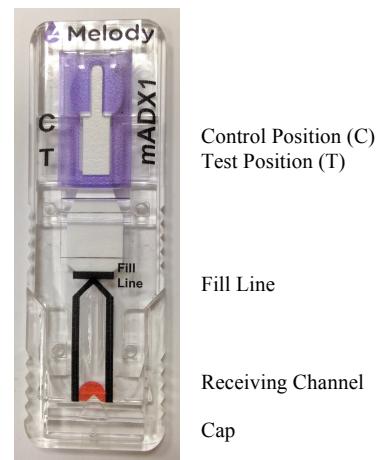
Ascendant Dx' first product, Melody™, to be brought to market is a tear-based diagnostic screening method for early detection of breast cancer. Melody™ can accurately diagnose malignant breast masses from the protein profiles present in tear samples. Results from initial clinical studies of sixty cancer patients and ninety healthy control patients show that combining a three biomarker panel can accurately predict cancer with ~80% specificity and 90% sensitivity. These proteins are present in the tears of women with all densities of breast tissue. While women with dense breasts (Category 3 and 4) are more prone to have difficult diagnoses of breast cancer via mammograms and have a four to six time increased risk of breast malignancies, we believe that Melody™ can provide an accurate test for breast cancer in all women.

Secondary product plans will be to examine use of Melody™ to monitor patients undergoing radiation and/or chemotherapy for breast cancer. We believe that the same proteins present in the tears of newly diagnosed patients will also be increased in patients where treatment regimens are not effective. Thus, clinical trials will be done to examine whether Melody™ can be used to examine breast cancer treatment and prognosis.

Melody™ will also be examined in additional studies to follow women who have been cancer-free and whether the Melody™ proteins present in their tears could be used to diagnose any possible recurrence of the disease.

Both the Melody™ treatment prognosis and recurrence studies will piggy-back on the clinical data collected from the diagnostic clinical trial described above.

The breast cancer detection platform Ascendant is developing with our partner, Now Dx, is a simple multiplex protein array. Ascendant has a joint development agreement with Now Diagnostics ([www.nowdx.com](http://www.nowdx.com)) to create a simple microfluidic platform for protein detection from tears. A prototype of this device is shown in Figure 1.



**Figure 1:** The Melody Prototype Device is a one-step detection method in development for three to five breast cancer markers isolated from tears.

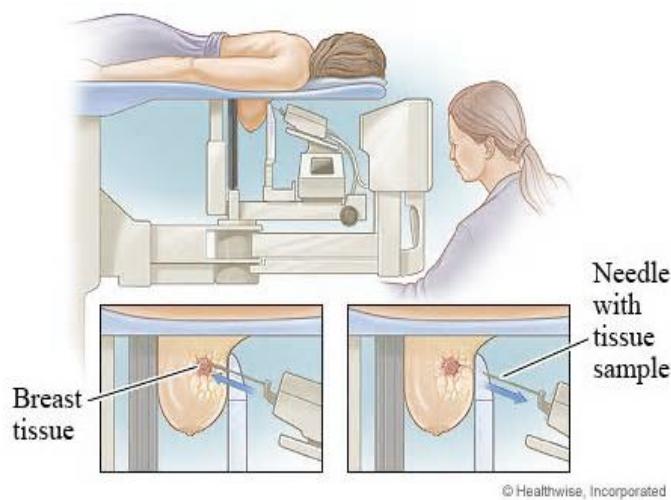


### Why Breast Cancer?

Approximately 240,000 women are diagnosed with breast cancer each year in the United States, with a 16% mortality<sup>1</sup>. In Canada, 24,400 new cases will be diagnosed each year with a 20% mortality rate<sup>2</sup>. The most effective method of reducing deaths due to breast cancer is to increase early detection rates. Recent statistics put the five year survival rates for stage I breast cancer at 93%, while stage IV survival drops to 15%<sup>3</sup>. Early detection currently available to women are clinical breast exams and annual mammography screenings, however these techniques only reduce mortality by 25-30% in women ages 50-69 and 17% in ages 40-49<sup>4</sup>. False positive rates vary but are usually around 5% per mammogram. Given the number of mammograms one individual will have in her lifetime, there is 50% chance of at least one false positive<sup>4,6</sup>. Given these statistics, participation rates in yearly imaging have plummeted to 50%<sup>5</sup>. Altogether, this creates a dismal outlook for the breast cancer continuum of care and increasing early screening rates using the current gold standards for screening.

### Breast Cancer Continuum of Care

The established breast cancer continuum of care pathway starts and ends with screening mammography. When an area of abnormality is observed on a screening mammogram, the patient is called back for a diagnostic mammogram and possibly an ultrasound. If the area is still suspicious, a biopsy is ordered and the tissue is sent to a pathology lab to determine if malignant cells are present. In the US over \$1.6B is spent on unneeded biopsies each year.



**Figure 2:** Mammography is the current gold standard for breast cancer screening. Millions of dollars are spent each year on needless biopsies to confirm suspicious areas observed by mammograms.

Should the biopsy results be confirmatory for breast cancer, the patient must often then have a MRI. The MRI serves to more accurately image the area of suspicion and to determine the best course of action for treating the cancer. In an extremely efficient clinic, the time from

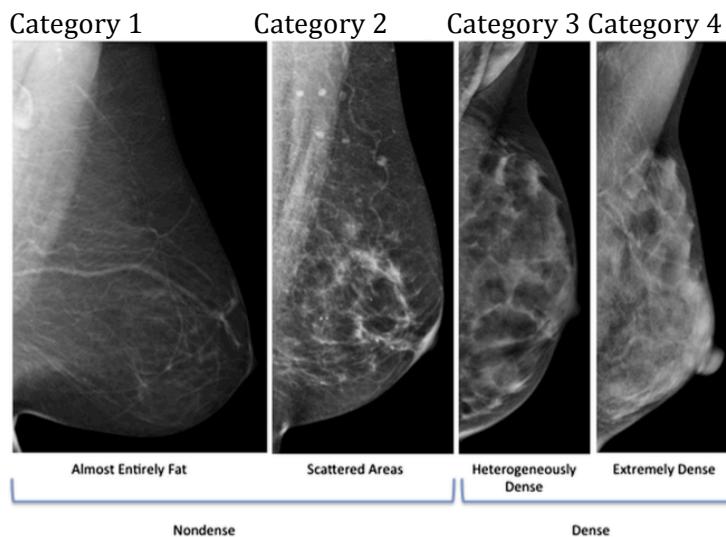


screening mammogram to treatment can be as little as two weeks, but often is much longer, even up to seven weeks. If the biopsy results are negative the patient is still considered high risk, and must return for a follow up diagnostic mammogram in six months and is not considered out of danger until two years of normal mammograms have been obtained.

### Challenges to current imaging techniques

The presence of dense breast tissue causes an even greater challenge, as mammograms are less useful with dense tissue. Women can develop tumors that remain undiagnosed until the cancer is at an advanced stage. Mammography is routine tool used to determine the level of breast density and screen for breast cancer, but as breast density increases the sensitivity of mammography decreases. Approximately 15% of cancers are missed due to observer error, often as a result of tumors being hidden behind dense normal breast tissue <sup>5,6</sup>.

A scale developed by the American College of Radiology (ACR) Breast Imaging Reporting and Data Systems (BI-RADS) is used to report mammographic breast density using a score from Category 1 to Category 4 <sup>7</sup>. An almost entirely fatty breast is given a score of 1, scattered areas of fibroglandular density is 2, heterogeneously dense is 3, and extremely dense breast tissue is given a score of 4 <sup>5,8</sup>. Approximately 40-50% of women fall into categories 3 and 4 <sup>7</sup>. Prior to recent legislation passed in several states requiring patients to be informed if they have dense breast tissue, women were often not aware of their breast density BIRADS score <sup>9,10</sup>. Women with breast of Category 3 or 4 are four- to six-fold more likely to develop breast malignancies <sup>11</sup>.



**Figure 3:** Breast tissue of four densities from “Fatty” (Category 1) to “Extremely Dense” (Category 4). Dense breast tissue obscures tumors on mammographic screenings. Dense tissue appears white on a mammogram similar to tumor tissue <sup>8</sup>.



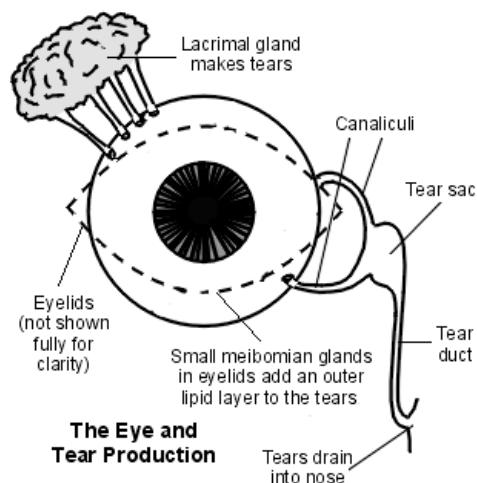
Follow up imaging techniques, such as whole breast ultrasound and MRI, are required to determine if any abnormalities may be present in these women. These procedures are much more costly than screening mammograms and are only covered in women who are considered high risk for developing breast cancer, i.e. strong family history.

A recent retrospective study Klifa (2010) did a comparative study to assess differences between 2D mammographic density studies and 3D Magnetic resonance (MR) density in a group of high risk women <sup>7</sup>. Results of this study indicated a difference between the two techniques. A woman who has fattier breast (less dense) shows minimal difference between 2D and 3D measures while a woman with denser breasts 2D results do not show the same conclusion as the 3D results.

To date, the biggest challenge to increasing the survival rate from breast cancer is accurate early detection such that therapeutic intervention can be initiated.

### Why Tears?

While the eye seems to be a fairly isolated organ, it has been documented that systemic affects also exert influence on the ocular environment. Studies suggest protein patterns in tears have the potential to generate biomarkers for disease state determination and could also provide new sources for treatment options and monitoring<sup>12</sup>.



**Figure 4:** Lymph tissue is present in the ocular cavity and releases lymphatic fluids into tears.

Tear fluid is secreted from the lacrimal gland and is responsible for keeping the eyes moist, preventing infections, providing nutrients, and serving as a barrier to the outside environment<sup>13</sup>. The typical total protein content in tears can be as high as 6-10 mg/ml, with a dynamic range from mg/ml to pg/ml<sup>14,15</sup>. Estimates of the tear proteome range from 500-1500 proteins, depending on detection technique, with a 35% overlap with the serum proteome<sup>16</sup>. Because the eye is an open organ, the composition of the tear proteome can be affected by environmental influences. In addition, tear proteome composition can be altered due to age, gender, time of day, food intake, and contact wear<sup>17-20</sup>. In order to obtain accurate disease specific information, as many of these variables as possible must be accounted for.

Histological evaluation of the ocular cavity has identified the presence of secretory components, specifically the lymphoid layer of the conjunctiva, indicating the conjunctiva is part of the secretory immune system<sup>21</sup>. The lacrimal sac and conjunctiva both have high endothelial vessels suggesting a mechanism for migration of lymphocytes from the blood stream into lymphatic tissues<sup>21</sup>. This participation



in the action of the immune system by ocular tissue, suggests an influence on the ocular proteome due to various disease states – including breast cancer.

There have been several diagnostics companies that have started in the past five years using tear fluid as the sample for diagnostic tests. Tear Lab and Advanced Tear Diagnostics are two examples of companies that combine tear samples and a point of care device to detect different proteins in the eye in order to monitor and diagnose a variety of ocular disorders. Advanced Tear Diagnostics, headquartered in Birmingham, Alabama, has a unique testing platform that is the first of its kind to receive FDA approval as a diagnostic for testing tears. This platform consists of a compact microarray system that provides quantitative test results for two tests (lactoferrin and IgE), shown to be involved in dry eye syndrome and inflammation, respectively. Tear Lab, of San Diego, California, has developed an osmolality system that can test a patient to determine if they have dry eye syndrome. Both of these companies use proteins found in tears to determine if a patient has a particular external ocular disorder.

### How does the Melody™ test work?

Tears provide insight into molecular events occurring within the body. Collection of tears is easy, non-invasive, and has relatively low risk to the patient. If tears are not being produced, which is rare, a saline wash of the eye can be employed. The pathway from tears to results is simple. A piece of filter paper, called a Schirmer strip, is placed in the lower eyelid. Participants are then asked to close the eye and keep it closed for a period of five minutes.



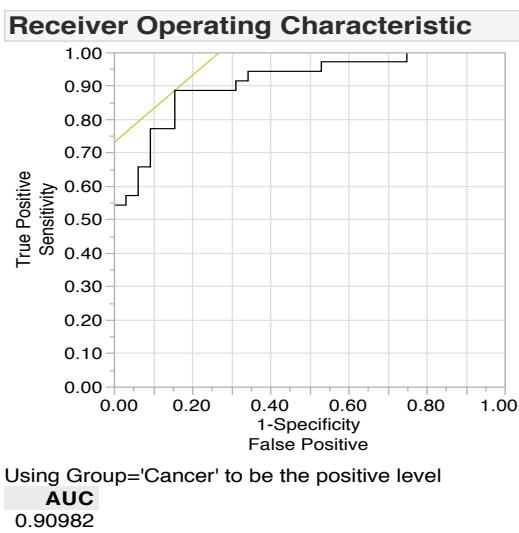
For most participants the initial discomfort dissipates within the first 10 seconds after which they often cannot tell that the Schirmer strip is still in place. The presence of a foreign object in the ocular cavity prompts the tear glands to produce fluid and it is this fluid, and the proteins within it, that absorbs to the Schirmer strip. To study the proteins, they are removed from the strip in a different solution and analyzed using various proteomic techniques.

**Figure 5:** Schirmer strips have long been used to diagnose dry eye. Ascendant Dx will use this method to collect proteins present in tear fluid for evaluation.

The proteomic technique we selected for the discovery phase was proteome wide analysis using Liquid Chromatography Tandem Mass Spectrometry. In this technique, enzymes are used to cut all of the proteins present in the tear samples into smaller protein pieces, called peptides. These peptide pieces are then separated out and identified by the mass spectrometry instrument. A software package takes that information and re-assembles the proteins based on the peptides that were identified. By comparing how much of each peptide is present in each grouping of samples we can determine how much of that peptide's parent protein is in the sample group.



Using statistical software, Ascendant identified a list of over 400 proteins present in the tears of breast cancer patients. Further studies hone the list to ~100 proteins via the further use of Mass Spectrometry. The proprietary proteins chosen to use in the Melody™ platform were further validating conducting a small clinical validation trial. Tears from up to 90 healthy volunteers and cancer patients were analyzed for proteins of interest from the list. We utilized Enzyme-Linked Immunosorbent Assays (ELISAs) to show that the combined use of three or more of the identified proteins was able to accurately determine which samples were from cancer patients and which were from healthy controls with a confidence level of 80-90% (Figure 6).



<b>Sensitivity</b>	88.57%
<b>Specificity</b>	<b>78.13%</b>
Positive Predictive Value	81.58%
Negative Predictive Value	84.48%

**Figure 6:** Preliminary data for Melody™ panel tested on 60-90 patients each from control and cancer populations. Data indicates Melody™ provides statistically significant differentiation of control from cancer tear samples. The

markers are apparent in tears from patients with all breast densities and breast cancer types, and >40% of samples tested are from patients with dense breasts. Data is from validation studies done with ELISA assays combining several makers identified by Ascendant.

The final Melody™ product will consist of two kits:

- ◆ consumer/patient kit containing a Schirmer strip for sample collection and
- ◆ kit for conducting evaluation of the proteins using a microarray technique which can be connected to a digital reader for quantitation and electronic records maintenance.

This second kit will be used in a clinical lab setting and will be partnered with diagnostic parameters for data interpretation.



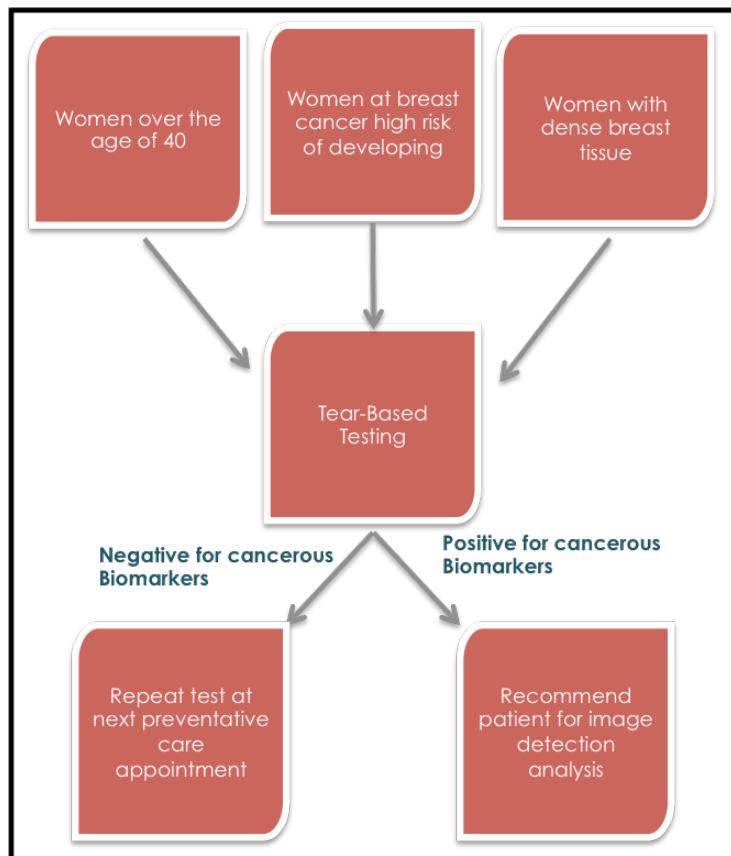
## ◆ MARKET AND COMPETITION

### Market Overview

The US diagnostic testing market has a projected value of \$98.4 billion in 2017. The *in vitro* diagnostic testing market specifically has shown particular promise and is expected to grow at an annual rate of 5.4% and reach \$74 billion worldwide by 2018<sup>1</sup>.

### Target Market

Yearly mammography screenings are recommended for all women over the age of 40 and individuals with high risk are encouraged to start screening even earlier, this demographic will be the primary target for tear based testing. There are currently approximately 70 million women age 40 and over in the US. Tear collection will be carried out by patient's primary care physician, internist, or OB/GYN. We anticipate the Melody™ test will be initially



**Figure 7:** Flow chart indicating incorporation of tear based screening into early preventive care screening for women over 40, with dense breast tissue, and with high risk of developing breast cancer.



performed in the clinical labs associated with the physician's office. Our ultimate goal is to prove the test is safe and effective at diagnosing breast cancer, such that in the future it can be provided as an over the counter or point of sale diagnostic. According to the department of labor, there are currently 99,000 General Practitioners, 48,000 Internists, & 20,000 OB/GYN's in the US.

### Established Competitive Market

Currently the most frequently used diagnostic tests for breast cancer includes conventional mammography, full-field digital mammography, whole breast ultrasonography, and breast MRI. Established competitors include GE health care (31% market share), Hologic (54%), and Siemens (15%) for mammography systems and up front costs can be \$300,000 to \$400,000 each.

### Developing Competitive Market

In the past decade several companies have developed tests for the diagnostic and predictive breast cancer market. Many of these tests are genomic assays that assess a patients overall risk of reoccurring breast cancer. Generally, patients who are HER or ER positive have more treatment options, therefore, having a more advantageous outlook when compared to patients who have triple negative breast cancer (negative for HER, PR and ER). However, several tests including Oncotype Dx, Mammaprint, and PAM50 are now FDA and CE approved and available on the market in the US as well as other countries<sup>22</sup>. These genomic tests provide risk assessment information on the potential for reoccurrence for specific sub-types of breast cancer.

Three genomic assays are commercially available for early stage risk assessment of breast cancer. Oncotype Dx determines the likelihood for distant recurrence after tamoxifen or aromatase inhibitors<sup>23,24</sup>. Results are provide on following information: the likelihood that breast cancer will return, whether you are likely to benefit from chemotherapy, and whether you are likely to benefit from radiation therapy if you are being treated for DCIS by giving a reoccurrence score that is categorized into one of the following categorizes (low, intermediate and high risk). This test has been validated on women who are hormone receptor positive, have early stage (I or II) breast cancer, and who have been on tamoxifen. Oncotype Dx tests RNA samples from fixed embedded tissues taken at time of surgery or biopsy and compares them with samples taken after treatment. This test is a 21gene, real-time, PCR assay used with a logarithm to determine the likelihood of breast cancer reoccurrence<sup>22</sup>. Oncotype Dx has a high false positive rating and there is no indication that it is better than the standard immunohistochemistry method. Both the American Society of Clinical Oncology (ASCO) and the National Comprehensive Cancer Network (NCCN) have incorporated this assay into their guidelines<sup>24</sup>.

Mammaprint, made by Agendia, is a 70 gene profile assay which was initially developed from a whole genome expression assay<sup>25,26</sup>. It was cleared in 2007 by the FDA and became the first breast cancer assessment test<sup>22</sup>. Unlike Oncotype Dx, this prognostic test is



independent of factors such as tumor size, receptor status, and HER2 status<sup>25</sup>. Mammaprint provides a high or low risk assessment of early stage breast cancer reoccurrence. This test has a high negative predictive value for distant reoccurrence after adjuvant treatment (both endocrine and chemotherapy).

Prosigna has developed a gene assay "PAM50" to assess the expression levels of 50 genes to identify the reoccurrence, risk category, and subtype of breast cancer<sup>27</sup>. This genomic test made by Nanostring, analyzes the activity of specific genes in early stage hormone receptor positive breast cancer patients. This assay recently became available in the United States. Prosigna is indicated for use in postmenopausal women with hormone receptor positive, node negative (stage I or II) or node positive breast cancer to be treated with endocrine therapy<sup>27</sup>.

Provista has developed an early detection serum biomarker assay, "dtect dx"<sup>28</sup>. This ELISA based detects the following biomarkers in serum IL-8, IL-12, VEGF, CEA and HGF with a sensitivity and specificity of 88.9% and 86.7% respectively<sup>22</sup>. This breast cancer diagnostic test is focused on women under the age of 50 in and is done in conjunction with imaging. The data from these biomarkers along with selected characteristics is analyzed together in an algorithm that generates a value of normal or elevated risk. However, many women whom are diagnosed with breast cancer are over the age of 50. For women older than 50 the dtect DX assay is not robust. Provista is currently working on adding autoantibodies to the current biomarker panel to develop a breast cancer detection assay for women of all ages.

There is currently no standard assay or technology for diagnosing or determining risk assessment for breast cancer patients. Many of these genomic assays can take 3 days or longer to get results and require taking a second tissue sample in order to compare the original sample to a sample after treatment<sup>22</sup>. This is both extremely invasive and time consuming without giving definitive results to the patients. Provista early detection assay requires a specific set of patients and only provides normal or elevated risk results without definitive answers.

Melody™ Dx differs widely from these previously described tests. Melody™ Dx uses tears as a sample source as opposed to tissue or a blood sample. This is much less invasive and requires less time. Melody™ Dx assay has the potential to be general population screening test and not specific to one type of breast cancer or specific hormone receptor. Many clinicians support multigene/ multi-biomarker assays because they are an effective tool for making treatment decisions in early stage breast cancer cases. These assays are constantly evolving into improved screening/diagnostic methods.

### ◆ SALES AND MARKETING



### Regulatory Requirements

Ascendant Dx tear-based test will be designed and clinically tested to prepare the platform for use in a doctor's office or clinic. Regulatory filings with the U.S. Food and Drug Administration will be sought for this purpose. Concomitantly, CE Marking will also be sought to enable sales in certain countries outside of the U.S. Several of our strategic partners have CE Marking allowing sales of their components used in our platform in other countries. Ascendant plans to piggy-back on our partners approvals and manufacturing opportunities for our products.

### Marketing

Once regulatory approval is granted, Ascendant Dx will employ a three tier marketing strategy targeting physicians, 3<sup>rd</sup> party payers, and patients. This is a method currently employed by pharmaceutical, medical device, and durable medical goods companies. Presenting scientific data supporting the tear based method as a viable *in vitro* diagnostic test will also be done at medical conferences and trade shows. Most of our sales emphasis will focus on methods to promote our product to physicians, as they are the most important sales channel.

## ◆ FINANCIAL PROJECTIONS AND USE OF FUNDS

### Total Available Market

To calculate the TAM for Melody, we assumed a price ranging from \$99, an aspirational price for Melody to \$250 which is the price of a screening mammogram. There are genetic and proteomic tests that are priced in thousands of dollars, but we believe that what the market needs is a relatively inexpensive and accurate test. The details of these estimates are in Appendix 1. The TAM for a proteomic test like Melody is between \$1.5B to about \$4B annually in the US alone.

### Revenue Model

The revenue model as outlined in Appendix 1, is based on the assumption that Melody is CE cleared in the EU, where sales can be started, followed by sales starting in early 2018 in the US after FDA clearance. The assumptions also assume a margin of 40% and sales price of \$99 (the lowest price assumed in our analysis). Another assumption is that we will not add additional headcount for the sales team and all sales will be thru partner channels.

### Use of Funds

The financial projections for the next 3 years are included as Appendix II. We project that we are going to need a total of \$10MM for operations in the next two years. At the end of this period, we will have entered markets in both the European Union (CE Mark regulatory area), and US (FDA Clearance regulatory area). In addition to equity investment, we believe that we can attract significant government and charitable foundation monies and contracts for development of the Melody and Melody PoC platform.



The funds will be used for:

General operations of the firm,  
Costs associated with a long term, large-scale clinical trial of Melody,  
Costs associated with CE clearance of Melody in the European Union,  
Costs associated with FDA clearance of Melody in the US,  
Costs associated with development of Melody PoC device,  
Costs associated with Melody II: Prognosis test,  
Costs associated with Melody III: Recurrence test,  
Costs associated with investigating Melody platform for other cancers.

### ◆ COMPANY EXIT STRATEGY

Our preferred exit strategy is acquisition by a major medical diagnostics company.

Acquisition is common in the medical diagnostics market and often occurs upon reaching major milestones such as development of a CLIA protocol, prototype development, or market launch. Upon achievement of each milestone, we will entertain offers to sell Ascendant Dx to major diagnostic test providers.



## APPENDIX I-Financial Projections

### Total Available Market

Market	Market Size	TAM @ \$250	TAM @ \$99
Number of mammograms per year (Oct 1, 2015 - FDA)	39,024,566		
Number of unique patients (recall rate 20%)	32,520,472		
Dense Breast Patients (40%) - Total Initial Target Market	13,008,189	\$3,252,047,167	\$1,287,810,678
Screening Mammogram Once a year - 80%	10,406,551	\$2,601,637,733	\$1,030,248,542
Screening Mammogram Twice a year - 20%	2,601,638	\$1,300,818,867	\$515,124,271
<b>Total</b>		<b>\$3,902,456,600</b>	<b>\$1,545,372,814</b>

<http://www.fda.gov/Radiation-EmittingProducts/MammographyQualityStandardsActandProgram/FacilityScorecard/ucm113858.htm>

### Two-Year Budget

Task	1Q16	2Q16	3Q16	4Q16	Total 2016	1Q17	2Q17	3Q17	4Q17	Total 2017	Total 2018	Assumptions
HC1 - Core Melody	5.0	5.0	5.0	5.0		5.0	5.0	5.0	5.0			
HC2 - Remote Melody	1.0	2.0	4.0	5.0		7.0	7.0	7.0	7.0			
HC3 - SJIA/KD	0.5	0.5	1.0	1.0		1.0	1.0	1.0	1.0			
Total HC	6.5	7.5	10.0	11.0		13.0	13.0	13.0	13.0			
Salary/Benefits	292.5	337.5	450.0	495.0	<b>1,575.0</b>	585.0	585.0	585.0	585.0	<b>2,340.0</b>		\$180k annual
Travel	19.5	22.5	30.0	33.0	<b>105.0</b>	39.0	39.0	39.0	39.0	<b>156.0</b>		\$1k month per
Legal/Regulatory - Clinical	25.0	25.0	25.0	25.0	<b>100.0</b>	40.0	40.0	40.0	40.0	<b>160.0</b>		
Regulatory - PoC	12.5	12.5	12.5	12.5	<b>50.0</b>	20.0	20.0	20.0	20.0	<b>80.0</b>		
Biostatistics - CRAB	50.0	50.0	50.0	50.0	<b>200.0</b>	50.0	50.0	50.0	50.0	<b>200.0</b>		
Accounting	1.8	4.8	4.8	4.8	<b>16.2</b>	10.0	10.0	10.0	10.0	<b>40.0</b>		
Capital Equipment	250.0	10.0	10.0	10.0	<b>280.0</b>	250.0	10.0	10.0	10.0	<b>280.0</b>		
SW/Cloud	5.0	5.0	25.0	25.0	<b>60.0</b>	30.0	30.0	30.0	30.0	<b>120.0</b>		
Consumables	50.0	50.0	50.0	50.0	<b>200.0</b>	50.0	50.0	50.0	50.0	<b>200.0</b>		
Kit Development - PMA	93.8	93.8	93.8	93.8	<b>375.0</b>	93.8	93.8	93.8	93.8	<b>375.0</b>		\$30 per Kit
Consulting	15.0	15.0	35.0	35.0	<b>100.0</b>	50.0	50.0	50.0	50.0	<b>200.0</b>		
PR/Marketing	25.0	25.0	25.0	25.0	<b>100.0</b>	50.0	50.0	100.0	100.0	<b>500.0</b>		
Patient Recruiting Costs	0.0	50.0	50.0	50.0	<b>150.0</b>	50.0	50.0	50.0	0.0	<b>150.0</b>		
Melody 2 - Prognosis R&D	0.0	0.0	62.5	62.5	<b>125.0</b>	250.0	250.0	250.0	250.0	<b>1,000.0</b>		
Melody 3 - Recurrence	0.0	0.0	62.5	62.5	<b>125.0</b>	250.0	250.0	250.0	250.0	<b>1,000.0</b>		
Ovarian Cancer	0.0	0.0	0.0	50.0	<b>50.0</b>	62.5	62.5	62.5	62.5	<b>250.0</b>		
<b>Total Expenditures</b>	<b>\$840.1</b>	<b>\$701.1</b>	<b>\$923.6</b>	<b>\$971.6</b>	<b>\$3,561.2</b>	<b>\$1,567.8</b>	<b>\$1,327.8</b>	<b>\$1,377.8</b>	<b>\$1,327.8</b>	<b>\$6,801.0</b>	<b>\$4,511.0</b>	
<b>Monthly Burn rate</b>	<b>\$280.0</b>	<b>\$233.7</b>	<b>\$307.9</b>	<b>\$323.9</b>		<b>\$522.6</b>	<b>\$442.6</b>	<b>\$459.3</b>	<b>\$442.6</b>			
<b>Revenue from all sources</b>					<b>\$1,125.0</b>					<b>\$1,398.0</b>	<b>\$7,437.0</b>	
<b>Fundraising needed</b>					<b>-\$2,436.2</b>					<b>-\$5,403.0</b>	<b>\$0.0</b>	



## Revenue Model

Revenue	CE						FDA										
	1Q16	2Q16	3Q16	4Q16	Total 2016	1Q17	2Q17	3Q17	4Q17	Total 2017	1Q18	2Q18	3Q18	4Q18	Total 2018		
Grant - SJIA/KD	\$0	\$0	\$850	\$0	\$850				\$175	\$175							
Grant - Melody	\$0	\$0	\$175	\$0	\$175				\$850	\$850							
AR R&D Tax Credit		\$100			\$100		\$125		\$0	\$125	\$0	\$0					
NRE	\$0	\$0	\$0	\$0	\$0				\$50	\$50							
Sales - CE	\$0	\$0	\$0	\$0	\$0				\$99	\$396	\$495	\$1,584	\$1,584	\$3,168	\$3,168	\$9,504	
Profit - CE									\$40	\$158	\$198	\$634	\$634	\$1,267	\$1,267	\$3,802	
<b>Unit Sales- CE</b>									<b>*1000</b>	<b>4000</b>		<b>16000</b>	<b>16000</b>	<b>64000</b>	<b>64000</b>	<b>160000</b>	
Sales - FDA											<b>107</b>	<b>428</b>	<b>1,711</b>	<b>6,843</b>	<b>9,088</b>		
Profit - FDA											<b>43</b>	<b>171</b>	<b>684</b>	<b>2,737</b>	<b>3,635</b>		
<b>Unit Sales - FDA</b>											<b>1080</b>	<b>4320</b>	<b>17280</b>	<b>69120</b>	<b>91800</b>		
Total												\$1,398	\$1,691	\$2,012	\$4,879	\$10,011	\$18,592
Profit												40% margin				\$7,437	

\*Assumption - CE Mark 3Q17

50% revenue share with NDX

Sales price PMA: \$250

Sales price NDX: \$99

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